專利藥廠與學名藥廠之專利訴訟策略

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摘要

製藥業是個錯綜複雜的產業，雖然研發新藥是一項高成本，技術密集且高風險的產業，但並非所有藥廠都以研發新藥為主要業務。整體而言，學名藥廠通常較不進行新藥的研發。就定義而言，專利藥廠或原廠係指其主要以研發新藥為其主要的業務，反之，學名藥廠則是以製造專利已過期之原廠藥為其主要業務之藥廠。以公眾利益而言，兩種藥廠都有其存在的必要，專利藥廠可持續提供藥品及其技術上的改良與創新。而學名藥則以更經濟實惠的價格提供較社會大眾，可靠且安全的藥品，對於醫藥普及與結省政府醫藥支出有著莫大的供獻。因兩種藥廠質上的不同而所產生的衝突為貫穿本文而持續出現的議題，本文將會以專利藥廠和學名藥廠如何以主張專利權等法律行為來達成各自的目地。即專利藥廠會以主張專利侵害等其它法律上的主張來阻止學名藥上市的時間來確保其市場獨佔，相反的，學名藥廠則希望在原廠藥專利過期後能及早上市來分食市場大餅。

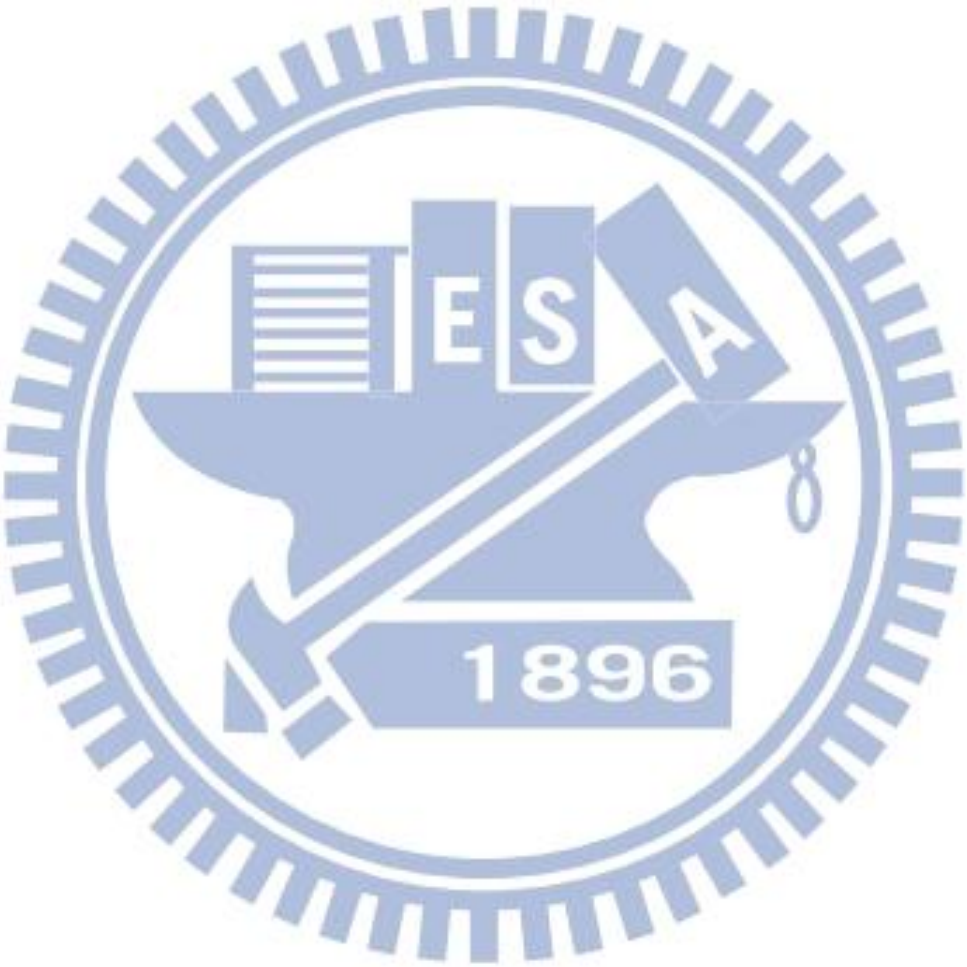
本文將以介紹製藥業的起源與其演變歷史為開始並對其產業特性加以著墨。後對美國藥品市場加及其早期藥品管制機制加以介紹。本文將以解析與批判 Hatch-Waxman Act 和專利連結制度（Patent Linkage） 為介紹美國法之重點。作者將對本法如何對藥廠間之訴爭可啟全新的戰場和訴訟策略加分析，自 Hatch-Waxman Act 以後，「處方用藥改善及現代化法案」（Medicare Prescription Drug Improvement and Modernization Act of 2003），為另一項指標性的立法。作者將會對本法如何成功的將數十年來因 Hatch-Waxman Act 所生訴訟的亂象改正加以剖析，分析其成功和未盡之處。

除美國外，本文亦對其它國家（澳洲，加拿大和韓國）對藥廠間的訴爭所採取修法上的措施加以分析比較。文末將加以參照台灣獨特的醫療環境和當地特色，這些當地的因素如何在藥廠中的抗爭中有著重大的影響。

最後，所然台灣尚未引進專利連結等美國法相關制度，然而各大跨國專利藥廠已經使用部份它們於美國常用的主張對抗台灣本土藥廠。隨著貿易持續性的開放與許多明星專利藥的陸續到期，藥廠間的訴爭應會持續燃燒。希望本文能提供台灣法院和立法者就藥廠間的訴爭有多一個觀察的面向和進而幫助立法者和法院

提出一個更符合當地需求的法律機制和判決論理的過程。

關鍵字：學名藥、專利藥、Hatch-Waxman Act、專利連結、專利訴訟策略、橘皮書



Patent Litigation Strategy between Generic and

Brand Name Pharmaceutical Companies

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ABSTRACT

Pharmaceutical industry is a complex business. While it is without a doubt that researching new drug is a capital-intensive and risky business; however, no all drug makers are engaged in this perilous endeavor. Broadly speaking, generic drug maker is an exception of this trend. By definition, pioneer drug maker, also known as brand name company, are referring to drug maker whose primary mode of business is engaging in researching new drugs; on the other side of the spectrum, is generic drug maker. Generic drug maker are pharmaceutical company that primarily engaged in manufacturing of known drugs whose patent term already expired. From public policy's perspective, both types of company are useful. Brand name company provides new pharmaceutical innovation and improvement; while generic company facilitates accessibility and provides more economically friendly drug to general public and healthcare provider alike. This conflicting interest will be the main theme throughout this paper and how brand name and generic company use litigation, especially asserting patent right, to further each their own interests i.e. Brand name will want to delay the entrance of generic drug into the market for as long as possible; in contrast, generic drug maker will want to market its drug as soon as possible.

This paper will begin by providing an introduction on the history of pharmaceutical industry and its unique characteristics that distinguish this industry from other business. Followed by an introduction on U.S. drug market and some of U.S.'s earlier attempt to control the conflicting interests between brand name and generic drug maker, this paper will start in earnest by providing a critical analysis on Hatch-Waxman Act and patent linkage system that comes with it. The author will comment on some of act's success and failure and how it opens an era of wild litigation battles between brand name and generic companies. Following Hatch-Waxman Act is another revolutionary piece of legislation known as "Medicare Prescription Drug, Improvement, and Modernization Act" which is American's attempt to fix problems and abuse created or

afforded by Hatch-Waxman Act. As will discuss in detail in this paper, while Medical Moderation Act did successful in eliminating some of the problems that have plagued Hatch-Wax Act for decades, some of its problem remain unresolved and some of act's half measure inadvertently opens door for more abuses.

However, U.S. is certainly not the only country in the world that had become battleground for pharmaceutical companies. This paper will provide a comparison of different regulatory regime implemented by Australia, Canada and Korea to combat these problems. In the latter part of this paper will present some of uniquely Taiwan element that will play a significant role in re-balance the interests.

Finally, though Taiwan have yet to fully adopt the American system in controlling drug marketing process, many of the multinational brand name company have already tried their legal tactic used in States in Taiwan's court. Hopefully, this paper will provide some observation to Taiwan's court and legislators when or if Taiwan decides to fully implement American system.

Keywords: generic drug, brand name drug, Hatch-Waxman Act, patent linkage, patent litigation strategy, Medical Moderation Act, Orange Book.

誌謝

Out of the night that covers me,
Black as the pit from pole to pole,
I thank whatever gods may be
For my unconquerable soul.

In the fell clutch of circumstance
I have not winced nor cried aloud.
Under the bludgeonings of chance
My head is bloody, but unbowed.

Beyond this place of wrath and tears
Looms but the Horror of the shade,
And yet the menace of the years
Finds and shall find me unafraid.

It matters not how strait the gate,
How charged with punishments the scroll,
I am the master of my fate:
I am the captain of my soul.

-By William Ernest Henley¸ "*Invictus*"-

這首詩是在偶然的情況讀到的，是鼓勵人永不放棄的精神，現在回頭看看正是我求學的寫照。現在畢業在即，回頭看我的曲折卻有充滿轉折的求學之路，對這一路上扶持我的父母，師長，同學及眾多貴人們，心中充滿無限感激！

首先感謝口試委員和劉老師能在這麼短的時間內安排口試，程序上也很感謝所辦助理們能在一片兵荒馬亂之際大力的幫忙口試事宜，能順利完成口試真是多虧大家的幫忙與配合。此外要特別感謝 徐壁湖大法官，除破例當任我的口試委員外，還花費許多保貴的時間幫我逐字校閱論文，在此特別感謝！

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在就學期間有幸的能進入公司服務，感謝筱君協理對配合我完成學業寬容的態度及多位同事對我平時對我的照顧，特別感謝洛枚，她的智慧與關懷溫暖了寫論文時的孤寂及安撫我的心靈。

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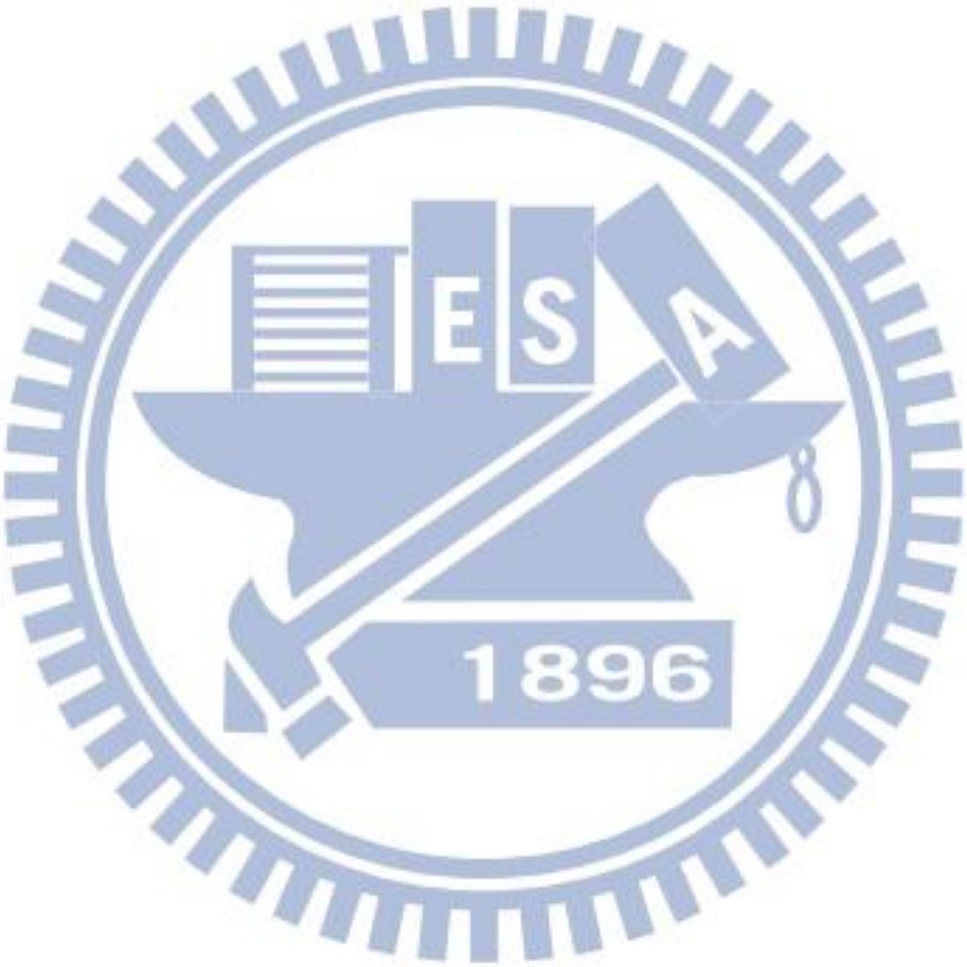

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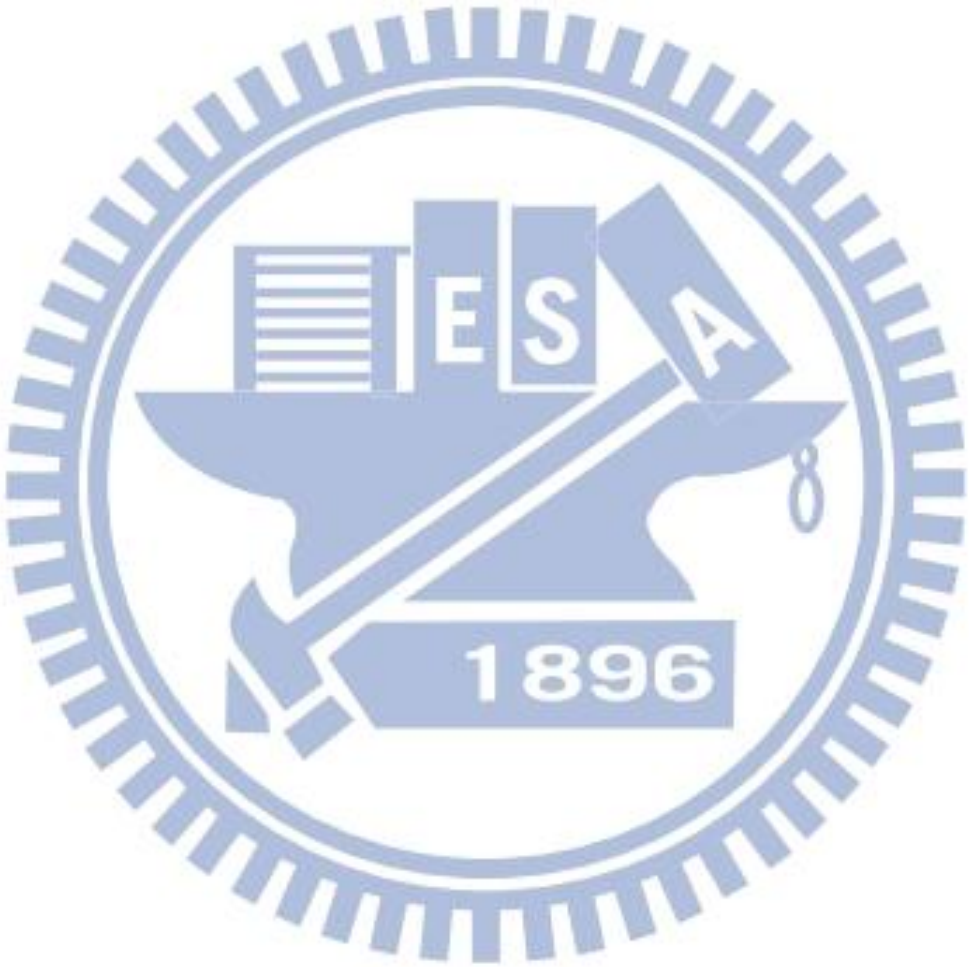

Chapter 1: Introduction, Research Purpose and Methodology

1.1 Introduction, Research Purpose and Methodology

There is no double drug industry is a capital intensive and highly competitive business. Despite its high cost, it is also one of the most lucrative businesses. In US, pharmaceutical company consistently rank among top ten in Standard and Poor's 500 index in New York stock exchange. Fortune magazine ranks pharmaceutical companies are on average, three times more profitable than any other company within fortune 100.[1] According to same magazine in 2002, the top ten pharmaceutical companies' total annual revenue (359 billion USD) is more than the revenue of rest 490 companies (337 billion USD) in Fortune 500 combined.[2]

Moreover, since 2005 there are more than 13 blockbuster drugs whose patents are about to expired and more than half of top one hundred innovator drug's patents are about to expired too. [3] That is more than 500 billion of market value up for grab for generic manufacturers. In Taiwan, generic drug accounts 68.7% for prescription drug expenditure, only 31% is on innovator drugs i.e. brand name drugs.[4] In light of Taiwan's active generic drug sector, with the advent of many prominent innovator's patent being expired, one of such is Viagra from Pfizer which is the 6th greatest selling

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[1] Marcia Angell 著，曾育慧譯，藥廠黑幕，頁 16（2006）。

[2] 同前註，頁 41-42（2006）。

[3] 蕭詩婧，總額預算下，台灣學名藥市場的策略研究----以降血脂劑（statin）為例，陽明大學醫務管理研究所碩士論文，頁 1（2005）。

[4] 朱榮宗，台灣製藥產業診所藥品行銷之探討－以 S 藥廠為例，逢甲大學經營管理所碩士論，頁 7（2008）。

drug under Pfizer with market value in the neighborhood of 20 billion U.S.D in 2012.[5]

1.2 Methodology

Author uses a qualitative approach to study jurisprudence and competition maneuver stemmed from the manipulation of intellectual property rights in pharmaceutical sector. The research is conducted by collecting, sorting and analyzing prominent judgments and holding from Federal Courts of United States and courts of Taiwan coupled with literature review gathered from various sources such as thesis papers, professional journals, periodicals, law reviews and news clips. Author will also perform case analysis on the change of regulation and analyze its impact on competition behaviors. A portion of this thesis will be on analyzing and pointing out potential exploits by drug manufacturers on existing regulations.

[5] 「威而剛專利失效，輝瑞砸 100 億美元拉抬股價」，鉅亨網新聞中心網站：http://news.cnyes.com/Content/20130628/KH8K8JJSHP2EE.shtml?c=us_stk（最後點閱時間：2013 年 6 月 28 日）。

The research procedure as follow:

Data Collection:

Sources include:

1) Cases gathered from District and Federal Courts of United States. Also cases from Taiwan Courts and Prosecution Offices.

2) Thesis papers, official bulletin and government regulation from multiple countries.

3) Professional journals, law review and articles from various sources.

1.3 Literature Review and Analysis

Perform analysis from following aspects:

1) Case analysis including its legal question, impact of its holding on industrial behaviors.

2) Analyzed changes in government regulations and their impact on competition behaviors.

3) Comparison of different competition strategy including use of different IP strategy by different drug manufacturers.

1.4 Litigation Strategy Review and Analysis

1) Summarize and perform critical analysis on intellectual property litigation tactics

2) Summarize and analyze different litigation challenge a generic drug manufacturer may face at different stage of its product development.

1.5 Research Outcome Analysis

1) Summary of research outcome and a comparison of different legal system used by different country in their attempt to remedy the problems resulted from patent linkage.

2) Issues that remain open to this day and lesson Taiwan can learn from its American forerunners.

Chapter 2: Development of Pharmaceutical Industry

2.1 Development of Pharmaceutical Industry

Pharmaceutical industry doesn't really come into the existence until the turn of 20th century. The first documented drug company was Merck and Schering in Germany in 1840, followed by Hoffmann-La Roche of Switzerland, Burroughs Wellcome of England, Etienee Poulenc of France and Abbot, Smith Kline of America during the period of 1830 to 1930.[6] Many of these companies were founded by pharmacists while some others such as Agfa, Bayer of Germany, Cib, Sandoz of Switzerland, Imperial Chemical of England and Pfizer of America, were started out as chemical companies before turning into pharmaceutical business. The combination of chemical synthesis and pharmacology were to become the driving force for the next phase in pharmaceutical industry.

During the period of 1930 to 1960, pharmaceutical industry was at buzzed for the new discovery of Penicillin, a new and very powerful anti-biotic, which is hailed as one of the greatest discoveries in pharmaceutical history. In 1953, human DNA's double helix structure was discovered. This discovery led pharmaceutical research into a new direction. As pharmaceutical industry starting to gain more attention from public so is government control. Food and Drug Administration is formed and given sole jurisdiction over pharmaceutical research and market approval in the U.S. In addition, "Federal Food and Cosmetic Act" (FFDCA) was also established and approved by Congress in response to

[6] 羅淑慧、陳麗敏著，亞太地區藥廠成功轉型經驗予我國之借鏡，頁 7（2009）。

the need of greater control over pharmaceutical industry.

From 1960 onward to 1980, pharmaceutical industry entered into a golden of research, many influential drugs were discovered during this period, to name a few: oral contraceptive, sleeping pill (Valium), tranquilizer (Librium). This period was also marked with increase of governmental monitoring of manufacturing process and equipment and lab/factory condition, these new regulatory measures are later come to known as "Good Manufacture Practice" (GMP) standards.

During 1980's, Hatch-Waxman Act and Orphan Drug Act were passed. These new acts will later play an influential role in global pharmaceutical scene.

Orphan Drug Act provides applicant, whose drug is for treatment of rare disease, which is defined as disease with less than 200 thousands patient population, a more speedy market approval process and was given 7 years market exclusivity regardless of its patent status as an incentive. Furthermore, once successfully approved, drug manufacturer is able to recoup up to 50% of expenses on clinical trial via tax reduction. [7] In 1984, Drug Price Competition and Patent Term Restoration Act, also known as Hatch-Waxman Act (HWA) was passed by Congress. This Act is the fruition of near a century of long struggle between generic drug and branded drug companies. In the past, for a generic drug to obtain market approval, the applicant will need to conduct clinical trial that is the same scale as its branded drug counterpart despite the fact that branded drug may have been on the market for decades. Consequently, due to the inherent high costs for these trials, few generic drug companies were able to meet such requirement. As

[7] *Id.* at 8.

the result, during 80's there are close 150 branded drug whose patent terms had already expired but with no generic version on the market to compete with them. [8] Hatch-Waxman Act is an attempt to strike a balance between the needs of continuing research and the need for more affordable drug pricing for the sake of maximizing public good. This act heralded a "Warring Period" between generic and branded drug manufacturers and marked the beginning of increasingly more common practices of extending patent term via cunning manipulations on patent construction, FDA and HAW regulations or using stalling tactic to prevent generic drug from entering the market in order to secure a "de facto" monopoly. These manipulations of extending one's patent term beyond as originally intended period is also known as "patent evergreening"[9] practice.

1990's is the golden days for pharmaceutical industry, at beginning of 90's, a drug with 5 billion USD annual sales can be considered as a blockbuster drug. However, as many prominent researches began in last decade i.e. began in the 80's are turning into overwhelmingly profitable product, such as HMG-CoA aka Statins, an effective agent in lowering cholesterol, Selective Serotonin Reuptake inhibitor (SSRI), commonly used in treatment of depression and is the active ingredient of Prozac. Take Statins as an example, there are several branded drug based on this family, such as Merck's Zocor (Simvastatin), Novartis' Lescol (Fluvastatin) and Pfizer's (Atorvastatin). Top 9 of Statins class drugs generates more than 296 billion USD in 2000 and Lipitor

[8] *Id.* at 9.

[9] Robert Weissman, *Victory and Betrayal: The Evergreen Patent System of Pharmaceutical Company Tactics to Extend Patent Protections*, MULTINATIONAL MONITOR (Jun., 2002), http://www.multinationalmonitor.org/mm2002/062002/weissman.html.

(Atorvastatin) alone generates more than 1 billion USD in its annual sales.[10]

2.2 Merger and Acquisition of Pharmaceutical Industry

From year 2000 and onward, meager between companies is becoming increasingly more prevalent in pharmaceutical industry. Merger and Acquisition (M&A) volume reaches of a record high of 2233 billion USD in mere three month period from September of 1999 to January of 2001. There are several reasons behind this trend: 1) Increasing threat from generic drug 2) Patent expiration on their "blockbuster drug" 3) new types of drug i.e. biosimilar are increasingly looking more promising as a new type of drug. All these factors threaten branded drug's pre-existing market share.

As previously mentioned, patent exclusivity is at the root of branded drug's ability to maintain market share and thus it is the single most reliable factor in generating revenue for a branded drug manufacturer. Once a drug's patent expires, its market share will be highly vulnerable to generic drug competitors and its price will quickly plummet. With the advent of Hatch-Waxman Act and its subsequent amendments on Abbreviated New Approval Application (known as ANDA) procedure, coupled with a more restrictive regulatory regime over patent listing/delisting in Orange Book, generic drug's availability after innovator drug's patent expired is becoming increasingly more prevalent. Furthermore, since researching for a new drug is an arduous journey with no guaranteed returns. As P. Roy Vagelos, former CEO of Merck & Co., Inc. puts it: "Acquiring another company is an effective remedy when a company's product patents are about to expire but there is not enough eligible new drug to help maintain

[10] *See supra* note 6, at 10.

company's market presence."[11] For example, when Schering-Plough's 27 billion USD worth Clarityne, an anti-allergic drug faces its patent expiration, to keep its market presence Schering-Plough will need to market a new generation, which is unlikely in such a short order. At the same time, Merck's Singulair, a drug that helps with asthma by reducing swelling, still have years of its patent term left. If Schering-Plough is able to market them as a combination drug with its own Clarityne , it will effectively extend Clarityne's patent term. While it is a good business move, it is not without its benefits for patients, as Dr. Clifford Bassett, a New York allergist states:

"People with moderate to severe asthma often suffer from allergies as well," he said. "And we've seen the incidence of asthma double in recent years. So, with this, you have a super-convenient way to moderate the symptoms of both asthma and allergies."[12]

In other words, what the doctor is saying even though patients with allergy may not necessarily need asthma drug but such drug will help allergy patients who are also suffering from asthma-like symptoms triggered by allergy. So the underlining principle is such: it is better to have it and not used it than when need it but didn't have with the only catch being combination drug is more expensive than if consumer brought them separately to each symptom. Business-wise, however, M&A is an effective competition measure in the face of increasing competition and low yield from its new drug research with added benefits to be potentially beneficial to patients as well. However, not all combination of old drugs into new one is as effective as the marriage between Clarityne and Singulair.

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[11] 傑佛瑞・羅賓森著，廖月娟譯，一顆價值十億的藥丸：人命與金錢的交易，頁 43-44（2002）。

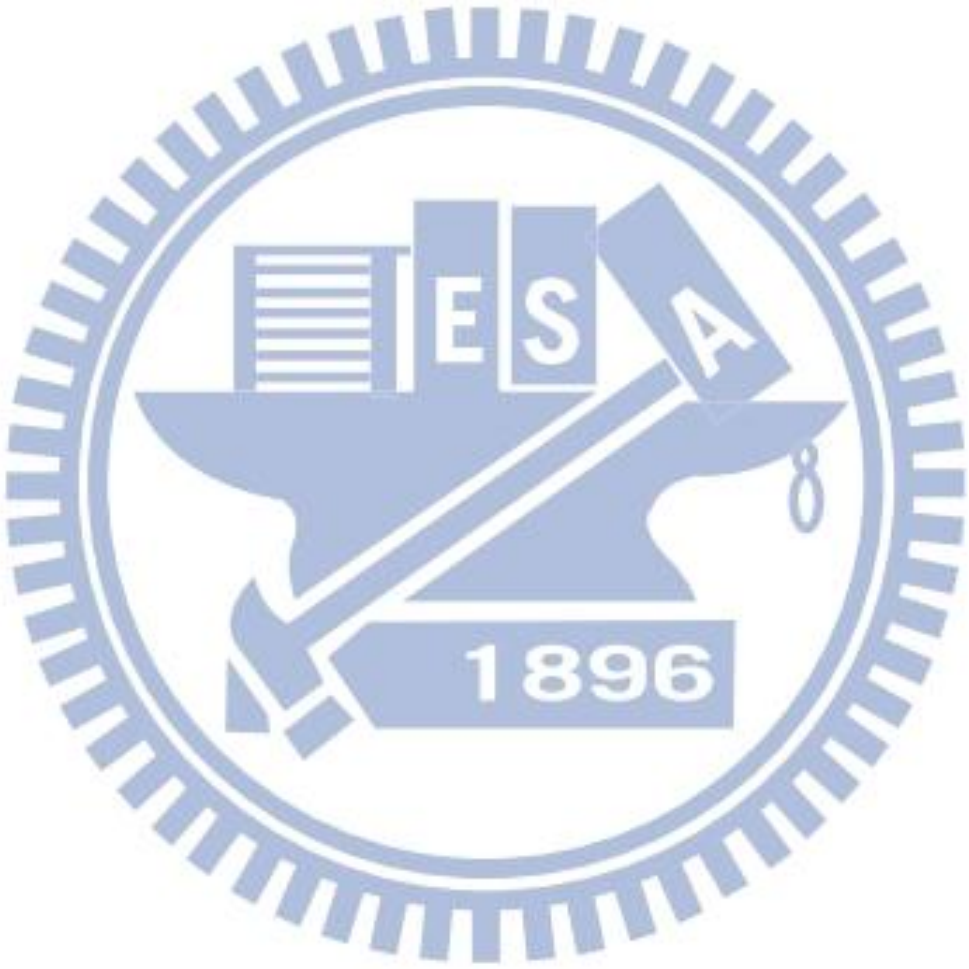
[12] Marrecca Fiore, *Allergist: Singulair, Claritin Combo Could Be Win-Win for Allergy, Asthma Sufferers*, FOXNEWS.COM(Aug.29, 2007), http://www.foxnews.com/story/0,2933,295062,00.html#ixzz21qRIbEyx.

Over the 78 new drugs that received FDA approval in 2002, only 17 of them have new therapeutic effects and only 7 of them were deemed to have provided "improvement" from their previous generations. In other words, the rest 71 out 78 new drugs were "me-too" drug i.e. drug that have similar therapeutic effect as ones that were already on the market.[13] These "me-too" drugs are able to satisfy the FDA efficacy requirement because FDA has a rather lax definition on efficacy. According to FDA, new drug isn't necessary "better" than the pre-existing drug as long as these drugs can demonstrate they are more effective than placebo and is different with its predecessor. Most common of these differences is modification in dosage regime such as change from daily to a weekly regime which is a form of "improvement" according to FDA standard. In other words, as long as these new drugs are modified from its own predecessor and are more effective than a placebo, such drugs will have a regulatory green light to enter the market.

As world changes so must pharmaceutical industry changes with it, brand name company copes with these changes by expanding product line also known simply as "Pipeline", incorporating new key technology from other company, expanding market share and all these goals can be achieved through M&A. The merger of Glaxo Wellcome and SmithKline Beckman in 2000 is another of such example. Back in 1994, SmithKline's 10 billion USD worth peptic ulcer treatment drug, "Tagamet" is facing patent expiration, not surprisingly, Smith Kline was eager to expend its product line in anticipation of the lost of Tagamet. To worsen the situation, Glaxo Wellcome had invested more than 20 billion USD in research in 1997 alone but its substantial investment yielded less than 5% market share on U.S. prescription market. Meanwhile, SmithKline sales on Tagamet had plummeted from 10 billion to 2 billion. The merger of

[13] *See supra* note 11.

SmithKline and Glaxo Wellcome allows the new company to have an even bigger research budget, 37 billions to be exact. [14] Furthermore, it allows Smith Kline, a British owned company to have a firm footing in US market.



[14] *Id.* at 53.

Chapter 3: US Market and FDA Regulation

3.1 US Market and FDA Regulation

Securing US market is essential for a multinational pharmaceutical company in terms of its revenue. As Duncan Moore of Morgan Stanley puts it: "… for any drug company, US market is a market they can't offer to ignore. It is one the fasting growing market and it worth nearly 40% on global prescription drug market. More importantly, 60% of world's drug company's profits are from US market." In 2007, US market is about 2865 billion USD, followed by Japan, then European countries (Britain, France, Germany, Italy and Span). Asian market (excluding Japan) is much smaller by comparison, but is increasing rapidly especially in countries such a China, India and South Korean. Its market increased by 25.7%, 13%, 10.7% respectively. According to IMS Health's estimation, 7 most promising markets or "Pharmerging Markets" that include China, Brazil, Mexico, South Korean, India, Turkey and Russia are expected to increase in annual rate of 12 %~ 13%. Industrial growth and implementation of national health insurance are significant factor attributable to this growth.[15]

Compare with other regional markets, U.S. market is one of the most profitable (average cost of perception for brand drug is $96; while average for generic is $29[16]) because there is rather lax regulatory control over drug pricing, on average, US version of the same drug is about twice as more expensive as it is in Britain. For example,

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[15] *See supra* note 6, at 13-14.

[16] Lisa M. Natter, *Infringement Lawsuits: The Continuing Battle Between Patent Law and Antitrust Law in the Pharmaceutical Industry*, 18 LOY. CONSUMER L. REV., 363 (2006).

Tamoxifen, a drug commonly used in preventing breast cancer, costs about 11.9 USD in Canada, 10.23 USD in Britain but 153 USD in the States. Furthermore, drug pricing is rather liberal at times, for example, Levamisole, a compound originally intent for lice treatment in sheep and was marketed at 0.06 per tablet. However, Levamisole is subsequently discovered to be rather effective in treating colon cancer in human as well. As the result, its price soars to 6 USD per table.[17]

For the next 10 years, pharmaceutical industry goes through massive re-structuring. Some prominent companies such as SmithKline, American Home Products, Roser, Sandoz were no more, in their place emerge Pfizer , Novartis and Sanofi-Aventis, these are later known as "Big Pharma". [18] In 1980, there are about 80 major pharmaceutical companies, after year of 2000, only about 35 of them left. Furthermore, in 2007, top 10 pharmaceutical companies constitute up to 41.3% of global market while top 20 constitute close to 58.3%.[19]

3.2 Pharmaceutical Industry and Market Approval in United States

As mentioned previously, United State is one of most significant market for drug companies. According to IMS health (a multinational firm specializes in compiling and distributing medical data especially ones related to pharmaceuticals), global drug market is about 4000 billion USD in 2003 and about half of sales numbers are generated from US. In other words, US market alone is worth close to 2000 billion in 2003 and with a rather lenient government intervention on drug pricing. By comparison, in

[17] *See supra* note 6, at 118.
[18] *See supra* note 11, at 43.
[19] *See supra* note 6, at 11.

Britain, drug pricing is determined by census from National Health Service (NHS), Department of Health and Drug Company. Drug pricing is also monitored by Pharmaceutical Regulation Price Scheme that is aimed to "achieve a balance between reasonable prices for the NHS and a fair return for the industry to enable it to research, develop and market new and improved medicines."[20] While generic drug pricing is determined by drug tariff which is a monthly publication on average market drug pricing and is used by NHS as reference in calculation of its payment for generic drug. Even under this elaborate pricing scheme with significant government intervention, branded drug is still very expensive. Of the total 108 billion USD NHS had spent on prescriptions in 2002, 97 billion was on branded drug while 55% of prescription was for generic drug.[21] In comparison, in United States, drug price is even higher in general about 60% higher than Britain.[22]

There is little government intervention on drug pricing because there is virtually no social compulsory healthcare insurance in U.S. with the only exception of Federal Medicare enacted in 1965 which originally did not incorporated prescription drug under its coverage as back in the days, drug pricing is relatively cheap and not consider a burden for most patients. It was not until 2003 with Medicate Modernization Act, did Medicare reimburse patient on prescription drug expense. However, no all citizens are eligible for Medicare, it is only available to citizens over age of 65 or people under 65 but with disability and are under Social Security Disability Insurance (SSDI). Some specific medical conditions such as end stage of renal disease will also help people to be

[20] NATIONAL HEALTH SERVICE, http://www.dh.gov.uk/health/category/policy-areas/nhs/medicines-nhs/pprs/(last visited May 21, 2012).
[21] *See supra* note 11, at 123.
[22] *See supra* note 11, at 122.

eligible into Medicare. In other words, most of people in US must reply on private insurance to supplement such an employment benefit package for their medical needs especially for prescription drug.

In drug manufacturer's defense, they contribute the higher drug costs in United States to the costs incurred during the extensive and expensive research and development period. While admitting drug price in America is significantly higher than in other countries because other countries enact regulatory scheme on drug pricing which inevitable transfer drug company's R&D costs to American patients as United States is the only country in the world that is willing and has the ability to bear such price according to Alan Holmer, a U.S. trade representative. In other words, for the world to continue to enjoy the benefits of new drug, the costs is inevitable and United States is only country in the world that is capable to pay for drug for their true value or so says the Big Pharms.

In summary, significant market size and liberal drug pricing which, of course, is also a contributing factor to U.S. market size and its comprehensive patent protection regulation partially due to strong U.S. lobby group such as Pharmaceutical Research and Manufacturers of America (PhRMA). These factors make US "The" market for multinational pharmaceutical company and an important focus for this paper since U.S. market is also where competition is most fierce both commercially and legally. Consequently, many of drug company's practices and maneuver in the area of intellectual property right manipulation and business competition originated from U.S. market are also being repeated by its subsidiary in its oversea market.

3.3 FDA Approval and Pharmaceutical Research

Currently there are three regulatory pathways to market a drug U.S. For new drug i.e. pioneer drug, manufacturer can apply under New Drug Application(NDA) 505(b)(1), for drug that based on a pioneer but with significant modification, manufacturer can apply for market approval via NDA 505(b 2) or apply ANDA for generic drug.

FDA will review all drug application based on two categories:

1) New Chemical Type or

2) The rest which include derivatives from known drug but with different manufacturers i.e. generics or drug that is based on known drug but offer improvements. For derivative drug that offers improve, its application will receive a “P” rating which will be listed for priority review. The rest will receive an “S” rating which means the drug has the same or similar therapeutic effects as those that were already on the market.

However, application of new chimerical type does not guarantee a priority review, some may not even have better therapeutic effect than existing drugs. Similarly, application that warrants priority is not necessarily new chemical type application. More often, existing drug with new formulate or other modification can offer improvements such as better therapeutic effect, reduced side effects etc.

In summary, there are three categories of New Drug Application, they are:

1) New Drug Application apply via 505(b)(1) and applicant must submit data collected from clinical trial for safety and efficacy review.

2) 505(b)(2) application where applicant is allow to rely at least partially on FDA's past approval data to prove new drug's efficacy and safety. Most drug apply under 505(b)(2) are based on existing drug but offer different dosage, strength, route of administration, dosage regime or indication.

3) Abbreviated New Drug Application (ANDA) under 505(j). ANDA applicant only required to conduct experiment to prove new drug is of "bio-equivalence" of pioneer drug or reference drug i.e. the drug ANDA drug is based on to satisfy FDA's efficacy and safety requirement .

3.4 Paper NDA

FDA's NDA 505 (b)(2) application pathway, also commonly known as Paper NDA allows drug manufacturer to enjoy market exclusivity or even patent rights but they must file a patent certification similar in ANDA but with less costs. In general NDA 505 (b) (1) will consider by most as the true "new drug" because it is for application with NME while Abbreviated New Drug Application (ANDA) is reserved for generic drug. NDA 505(b)(2) is the one in between the two spectrum. The approved changes to pioneer drugs that will be under NDA 505 (b)(2) includes:

1) Changes in dosage and strength
2) Changes in routes of administration
3) Substitution or modification on active ingredient e.g. salt, ester, etc.
4) New Indication
5) New combination with previously approved drug
6) Over the counter-switch of an approved prescription drug

For drug company who is applying through 505(b)(2) there are several advantages. Applying via 505(b)(2) is cost effective, creates new patent right that allows drug maker especially for brand manufacturer to continue its blockbuster drug's product line with the exception of biologic drug[23] which is mostly approved via Biologic License Application (BLA). 505(b)(2) allows the applicant to submit preexisting data from its other product or usually data from the drug's previous generation as reference, these data includes data from clinical trial. While FDA reserves the right to request additional pre-clinical, clinical trial or literature information need to support these new formulation/combination from applicant, it still presents tremendous saving for drug company. As for drug filed under 505(b)(2) its approval costs is about 3 to 7 million USD, comparing with approval cost for drug filed under 505(b)(1) which can costs up to 1.3 billion USD. [24] Moreover, under 505(b)(2) it allows drug maker to change its formulation or presents new combination of preexisting drugs to be eligible for new patents and market exclusivity (3 years).

Filing under 505(b)(2) is not a certain bet, for example in 2002 Pfizer filed a NDA via 505(b)(2) based on Dr. Reddy's Labs' amlodipine maleatetablets and in 2003 TorpharmPetition's (b)(2) NDA on Synthon's paroxetinemes. All of them were denied by FDA; however, (b)(2) NDA is still an increasingly practices for brand name company. In 2007, the number of new drug application filed under 505(b)(2) was about 43%. In 2008, more than half of the new drugs approved in the United States were based on the 505(b)(2) process. This number will be expecting greater than 90% in 2012.

[23] A substance that is made from a living organism or its products and is used in the prevention, diagnosis, or treatment of cancer and other diseases. Biological drugs include antibodies, interleukins, and vaccines. Also called biologic agent and biological agent.

[24] FDA Approval of Biologic Drugs under 505(b)(2) Expected to Increase http://www.typepad.com/services/trackback/6a00d83451ca1469e20153924aacb8970b

3.5 Chapter Summary

	505(b)(1)	505(b)(2)	ANDA
Review time	12 months	12 months	21 months
Scientific study	Full	Partial	Bio-equivalence
New Ingredient	Yes	Yes/No	No
New Formulation	Yes	Yes	Yes[25]
New Dosage	Yes	Yes	No
Patent	Yes	Yes	No
Market Exclusivity	Yes (5 years)	Yes (3 years)	No [26] (180 days)

One of the most profitable but also most challenging among these there is 505(b)(1) i.e. the development of a new drug. Developing a new drug is certainly a very arduous endeavor. A new drug on average takes about 15 years to develop and costs between 500 millions to 2 billions USD. A new drug's development can be divided into 4 phases: Discovery to Pre-clinical, Clinical, NDA Review and Post-Market Surveillance.

3.6 Discovery to Pre-clinical.

During the initial discovery phase, 250 most promising New Molecular Entity

[25] Very limited change.
[26] Yes when against other generic drugs.

(NME), among one of them will later be the active ingredient of a new drug, are selected from a sea of rough 10,000 possible compounds. Normally, a drug is consisted of binder or solvent or other additive that facilitates the delivery of drug into a human system or improved drug's retention by human body. Active Ingredient, as its name suggests, is the actual chemical entity that is responsible to the intended therapeutic effect of any given drug. Animal testing will be conducted with these NME. Among the 250 NME, roughly 5 of them[27] will be selected for clinical trial, discovery to animal trail will usually takes about 6 to 7 years to complete.

3.7 Clinical Trial

Before Clinical Trial, FAD will conduct a 30 days safety review. There are three phases within clinical trial, each phase with involved with ever more subjects. From 20 to 100 volunteers in phase 1, to 100 to 500 volunteers in phase 2 to finally 1000 to 5000 volunteers in phase 3. In phase one, the purpose is to establish new drug's optimal dosage by conducting trials on healthy people, in order to study the change of human metabolism due to the drug and observe side effects if any. Most often, it is during this phase that drug company will begin to apply for patents on innovations associated with the new drug. Timing on patent application is a dilemma for drug company: on one hand, company wishes to protect its innovation as soon as possible especially during the later phases of clinical trial with so many people and professionals involved, it will be virtually impossible to keep its innovation a secret. On anther hand, as soon as it applies for patent, new drug's patent term clock starts ticking and along with its precious time for market exclusivity.

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[27] 葉嘉新、林志六著，新藥開發與臨床試驗，頁 23（2008）。

In phase two, usually a comparison groups will be set by patients of the targeted illness and people who are already taking medication to establish new drug's efficacy. In phase three, an even larger scale of patients will be enrolled into the study to examine new drug's safety and efficacy with greater pool to account for possible different pharmaceutical reactions on different physiology. Not all drugs that approved for clinical trial will enter phase three, many are pulled out during phase one and two. Only drug that passed all three phases will be qualified to FDA market approval.

Clinical trial usually takes 7 years to conclude and gathered enough data to apply for a New Drug Application (NDA) review with United States Food and Drug Administration. FDA review procedure usually takes roughly one and half year to complete.

After drug has been approved for market, FDA will continue to monitor it for any adverse drug reaction when it is introduced to general public. Despite the people involved in clinical trial, it is still relatively very small with very limited variety of medical conditions comparing with general population. Post Marketing Surveillance allows both FDA and drug manufacturer to further refine and confirm the safety of a new drug.

3.8 Pioneer Drug (Brand Name Drug)

Pharmaceutical that is approved via a NDA is also known as brand name drug, pioneer drug or simply branded drug because such drug is usually first of its kind and has more than one patents associated with its active ingredient or other methodologies such as production techniques. Company that manufactured branded drug is usually

also the patentees for these patents and such company is known as brand name Company as they usually market new drug under a catchy commercial name such as Zentact, Lipitor and etc. so in a sense these drug is branded by the company. As mentioned, developing a new drug is a risky and costly business, among the NME that has successfully passed FDA safety review and eligible for clinical trial, only 11.6% to 16% of them successfully pass NDA review. Furthermore, not all drugs that enter the market are going to profitable. Under such dire and uncertain circumstance, when a drug that actually make substantial revenue for the company, it is only natural that brand name company will do all they can to ensure these so-called "blockbuster" drug stay on the market for as long as possible.

Blockbuster drug is an essential source of revenue for a brand name company. One blockbuster drug can account for up to 30% of a company's total revenue. In 2006, there are total of 114 drugs that can be considered as blockbuster drugs and each generates more than 10 billion USD in annual sales in U.S. alone. By comparison, Taiwan's pharmaceutical market is about 600 billion in 2009. These 114 drugs are hold among 30 pharmaceutical companies.

Despite brand name drug's ability to generate high revenue, pharmaceutical is not like other regular consumer commodity, there is little brand loyalty. Doctors and patients, most of the time, choose brand name drug simply because it is only one available. In other words, blockbuster drug's ability to generate high revenue is largely due to its market monopoly afforded by its patent right.

3.9 Generic Drug[28]

Generic drug, on the other hand, is referring to drug that is manufactured based on a brand name drug after its patent has expired. By definition, generic drug has the same active ingredient as the brand name drug it is based on, and it has passed bioavailability and bioequivalence (BA/BE) tests that certify generic drug has the same efficacy and safety as its brand name ancestor such drug is also known as the "reference drug" of the generic drug.

Bioequivalence Test

BE test or bioequivalence test is meant to test whether two drugs when introduce into human body (in vivo) under the same condition and same dosage, the difference in rate and extent of active ingredient available at drug's intended site or absorption rate within circulation between the two drug to be statically significant or not. If not, then the two drugs is said to be bioequivalence of each other. In other words, if two drugs are said to be BE with each other, they are "with respect to both efficacy and safety, [they] can be expected to be essentially the same."[29] BA or bioavailability is a measurement on the rate and extent of a drug's active ingredient or its therapeutic ingredient when utilized in a human circulation system. In summary, if a generic drug passed BA/BE test with its reference drug i.e. brand name drug, it shall be utilized by human body and achieve the same therapeutic effect as a brand name drug. Any difference between

[28] Generic Drug is defined as a pharmaceutical compound that contains the same "active ingredient" as its patented counterpart…. the generic drug is identical to the patented drug in terms of its bioequivalence, more specifically; the generic version of the brand name drug should have the same pharmacokinetic and thermodynamic properties. The FDA requires the bioequivalence of the generic product to be between 80% and 125% of that of the patented drug.

[29] Birkett DJ., *Generics – equal or not?*, Aust Prescr. 26:85–7(2003).

generic drug and brand name drug is, by definition, statically insignificant.

In U.S., FDA will assign an “AB” rating to generic drug that are bioequivalent to brand name drug. FDA defines bioequivalent of a generic drug that has the same: 1) active ingredient 2) dosage form 3) route of administration and 4) strength as its reference drug.

The FDA requires the bioequivalence of the generic product to be between 80% and 125% of that of the patented drug. The two drugs are said to be of bioequivalent if "they are pharmaceutically equivalent and their bioavailability (rate and extent of availability) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, can be expected to be essentially the same. Pharmaceutical equivalence implies the same amount of the same active substance, in the same dosage form, for the same route of administration and meeting the same or comparable standards." However if two drugs were said to be bioequivalent of each other, as in the case between generic and the innovator drug it is based on, it does not mean that two drug were identical with each other. In fact, many generic drugs may have different binders or other inactive components known as “excipient” in addition with the active ingredient. Consequently, chemically branded drug and generic drug will have slightly different properties with each other. Even among other generics drug of the same type will have slightly different formulation with each other to achieve different effects, curative or otherwise, such as better delivery etc.

3.10 Generic Drug’s Competitive Edge

Brand name drug certainly contributes greatly in improving general health;

however, it does not come cheap. Brand name drug industry is one of the most profitable industries in the United States. In 2005, of the total of 250 billions that were spent on prescription drug, over 229.5 billion were spent on brand name drug. Furthermore, the cost of drug is on a steady raise at rate of 14% to 18% per year from 2004 to 2007. Interestingly, while price for brand name increase by an average of 21%, in comparison, the price for generic drug actually decreases by an average of 12.8%. Brand name drug is expensive and maybe too expensive to more and more people. During the period of 2004 to 2008, the prescription number for generic drug increase by 12%, while number for branded drug decrease by 6% during the same period. Generic drug use has come a long way, from less than 20% of prescription in 1984 to 78% in 2010.[30]

Generic drug has several distinctive advantages over branded drug, generic drug is:

1) Substantially cheaper

2) Significantly easier to manufacture with little research & development effort

3) Has very high market erosion rate against branded drug.

One of the most obvious advantages of generic drug is its pricing. Generic drug priced substantially lower than brand name drug. 1998 Congressional Budget Office (CBO) concluded that by using generic drug instead of its branded counterpart part, it has saved consumers between 8 to 10 billion USD this year. Another study publish by Generic Pharmaceutical Association based on independent analysis of IMS

[30] C. Scott Hemphill & Bhaven. N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 1(2012).

(Intercontinental Marketing Services) Health's data, during the period of 1998 to 2008, by using generic drug instead of branded drug have saved 734 billion USD for average consumers and healthcare providers, about 121 billion USD were saved in 2008 alone.

Federal Trade Commission (FTC) estimates that first generic drug typically priced at about 70% to 80% of its reference drug when it first enters the market. As first generic drug's 180 days market exclusivity expires and more generic drugs enter the market, price will continue to drop. For example, Prozac, a popular anti-depressant that often hailed as one of the most popular drug after the invention of antibiotic. During its patent term, Prozac sells for 2.13 USD per capsule. After its patent expiration, the first generic version sells for 1.91 USD per capsule when it first enters the market, about 12% less than the brand name Prozac. Price plummet to 0.32 USD per capsule after first generic drug's market exclusivity expired.

Developing a new drug is never an easy endeavor, it takes average of 15 years and millions of dollar and provided if the research is successfully. Moreover, even if a drug company is able to conquer many obstacles and successfully obtains market approval, new drug will not necessarily guarantee a financial success. Generic drug, on the other hand, is a much safer and reliable venture financially. The catch is: As long as generic company can secure its supply of active pharmaceutical ingredient (API) manufacturer, generic drug only need to pass BE/BA test to obtained market approval and save its self all the costs in discovery and clinical trial. Unlike a lot of brand name companies who synthesize their own API and have direct control over its product from the initial manufacturing to final marketing. Usually General drug manufacturers do not synthesize its product's own API, they obtain their supply from manufacturers who

specialize in synthesis API. The source of API can be from plants, fermentation of microorganism or synthesis of chemical compounds. Currently there are about 4000 types of API on the market, 60% of them are generic drugs and rests of the 40% are for pioneer drugs. API can be further categorized into high tech-level API and low tech-level API. As its name suggests, High tech-level API is referring to API that requires sophisticated level of manufacture technique and equipment. For example, there are only 5 supplier of API in the world for Topotecan, a widely used active ingredient in cancer treatment. Low tech-level API referring to active ingredients that are relatively easy to make and usually are for drug that have been widely used, such as anti-inflammatory agent or anti-biotic.[31]

Not surprisingly, generic drug company represents the greatest client sector for API manufacturers since many brand name companies synthesize their own ingredients. The relationship between drug manufacturer and API supplier can be illustrated as a cook and his foodstuff supplier. API supplier provides raw material for drug manufacturer to "cook" into a dish i.e. a drug. Consequently, for a generic drug company the greatest challenge is to secure a reliable API provider, generic company's main contribution lies in devising a better delivery system or possible combination with other known drug and marketing, these activities, however, are a lot less time-consuming and capital intensive than researching for a new active ingredient. As the result, once a brand name drug's patent expired, generic drug company is able satisfy BA/BE test and market its version of branded drug in relatively a short time.

31 「台灣原料藥公司闖出一片天！」，財子學堂網站：http://www.caizischool.com/blog/4795（最後點閱時間：2013 年 7 月 6 日）。

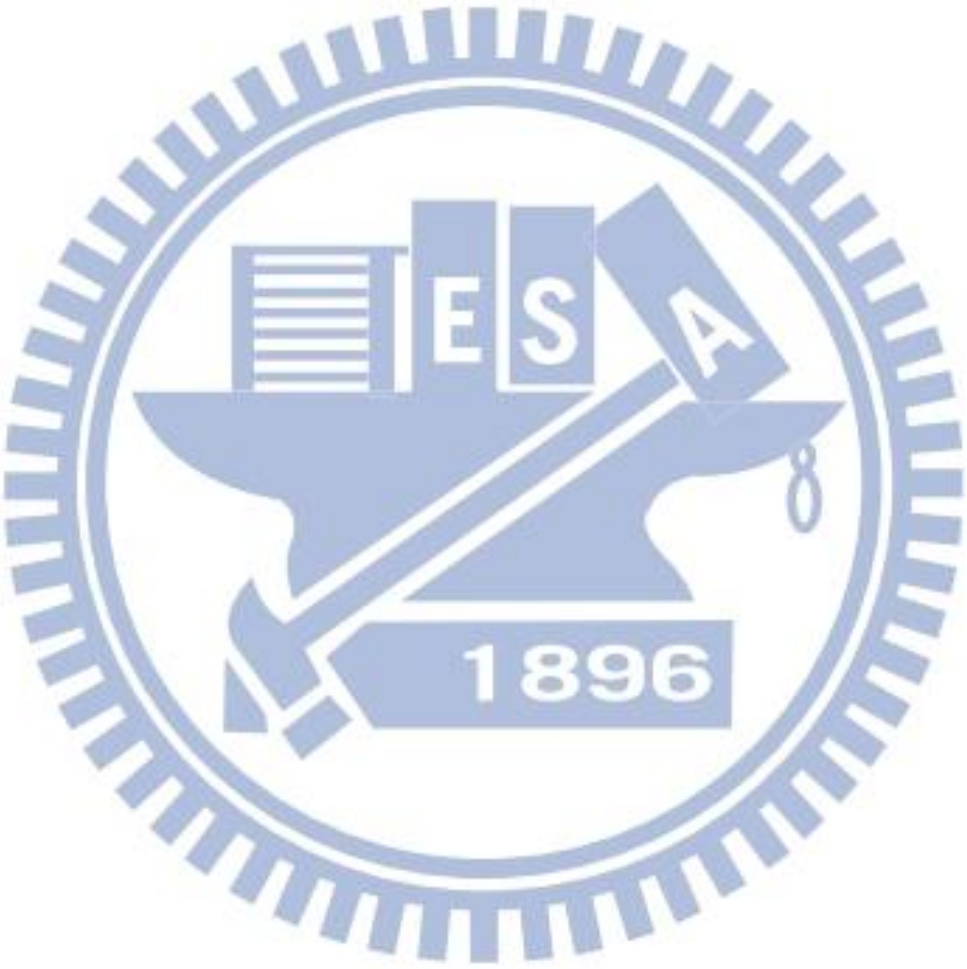
Since generic drug is cheaper and relatively easier to produce, it presents great threat to branded drug once it enters the market. Takes previously mentioned Prozac as an example; Generic Prozac claims 65% of market share from brand name company within a month after its introduction and close to 90% after an year. This outlines the basic dynamic within pharmaceutical industry. Brand name company specialized in pioneer drug which is expensive and difficult to make; however, once brand name company succeed in making a blockbuster drug it is going to bring tremendous revenue. However, the ability to bring revenue lies in its market monopoly granted by patent's exclusivity. Once branded drug's patent expires, it will lose its market share rapidly to generic competitors due to their cheap price. In other words, patent right is instrumental in branded drug's ability to generates revenue and it is only natural for brand name company to want these patents to be last as long as possible especially for their blockbuster drugs.

3.11 Costs for Pioneer Drug

While innovator drug a.k.a. pioneer drug is indispensable in furthering medical research and improve human health, it can also places significant burden on a country's treasury. For example, since the implementation of National Health Insurance (NHI) in Taiwan, from year of 2000 to 2007, expenditure on drug prescription constitutes to up 25% of total NHI budget and it is growing steady annually from 2% to 15%. [32] From a government's perspective, generic drug provides an enticing alternative that is able to provide drug that is as effective as branded drug but only 1/2 or even just 1/3 of the

[32] 湯澡薰等著，各國藥品支付制度及藥價政策分析及評估，行政院衛生署九十八年度委託研究，頁 1（2009）。

costs. Introduction of generic drug into a market helps greatly in stabilizing drug price. However, if government policy favors too greatly to the generic drug company, it may indirectly discourage research effort of brand name drug or in Taiwan's case discourage new drug from entering the market which in a long run is also detrimental to public's good.



Chapter 4: Pharmaceutical Patents and Patent Evergreening

4.1 Pharmaceutical Patents and Patent Evergreening

There is nothing more important and more profitable for a drug company especially brand name drug company to extend its market monopoly (usually via exclusivity right granted by patents sometime even through copyright claims). Following chapters will elaborate how drug companies have devise numerous strategies either through manipulation of FDA regulation or other intellectual property rights such as patents and copyright for the sole purpose of keeping out or at least delay generic drug from entering the market for as long as possible.

Generally just a single generic drug on the market will not present too much a threat to brand manufacturer since the first generic drug company usually price its generic drug just a little cheaper than brand name drug. However, all hell break loose especially for brand name company when other generic drugs are entering into the market as well, significant profits are at stake for brand name drug, more so if the drug in danger is a blockbuster drug. Entrance of generic drugs usually means billions of USD in profit will vanish within just couple months for brand name companies. Consequently, if a brand name company can stall entrance of generic drug even for just a few months, it will be highly profitable, usually worth many times over the legal expenses incurred during the process. As Stock Analyst, Hemant Shah said in Wall Street Journal: “Brand Name Drug Manufacturer’s counter-generic drug strategy is

perhaps the most profitable one in all of their other business ventures." [33]

4.2 Irony of Brand Name Drug's Innovation

Brand name drug company distinguish themselves from their generic counterparts in their capability in conducting research for new drugs. Bayh-Dole Act opens door for major drug company to utilize the research result including patent rights from National Health Institute (NHI), universities or other government- funded small business in the form of licensing. In other words, Bayh-Dole Act allows entity such as universities that received government funding for conducting research to have control over its intellectual properties.

Not surprisingly, fruit of research is a tempting subject for brand name company when its own research hits a dry spell which is increasingly more to be the case. Over one third of new drug that hit the market recently is based on patents licensed from NHI, universities or small biotech firm.[34] Taxol is one of such drug that is developed by government funding but brand name company is the one that is able to ripe its commercial benefit.

Taxol is the brand name of paclitaxel which is a medicinal compound gathered from pacific yew tree's bark. Taxol is one of the most popular drugs used in the treatment of lung and ovary cancer. It was originally discovered in 1960 and most of clinical research effort was conducted by National Cancer Institute (NCI) and subsequently gained FDA approval as an effective new drug for ovarian cancer.

[33] Chris Adams & Gardiner Harris, *Drug manufacturer step up legal attacks that slow generics*, WALL ST. J., July 12, 2001, at A-1.
[34] *See supra* note 1, at 39.

However, its patent right is licensed to Bristol-Myers Squibb (BMS) for 5 years of market exclusivity. The deal is controversial to say the least, as NCI, for all intents and purposes, gives BMS a practical monopoly on research founded mostly by the government, in other words, from tax payer's money. NCI defenses its decision because the financial scale needed to supply the tree i.e. the government alleges in order to ensure the raw material of paclitaxel meet the demands for general public the association of a pharmaceutical company as a commercial partner for marketing Taxol is needed. Regardless, BMS is the biggest winner in this bargain as Taxol's revenue is close to 10 billion USD.

Gleevec is another case where brand name company steps in to ripe the fruit of others' labor. Imatinib Mesylate which is brand named as "Gleevec" by Novartis. Gleevec is a revolutionary drug in the treatment of leukemia. Gleevec, however, is not developed by Novartis. In 1960, it was discovered people who has leukemia carry a unique set of chromosomes known as "Philadelphia Chromosome" which is responsible in triggering the production of abnormal enzyme that causes leukemia. Novartis had developed several enzyme inhibitors that may possible inhibited the production of these enzyme and applied for patents on all these inhibitors accordingly. However, no further action was taken by Novartis until Brian Druker of Oregon Health & Sciences University in Poland who is funded by National Health Institute. He discovered one of Novartis' enzyme inhibitor is practically effective in suppressing cancer cells while leaving the normal cells intact. This is when Novartis steps in and carry out the clinical trial. Gleevec hits the market after 2 years spent in clinical trial.

Government funded research plays an integral in developing new drug. At turn of the millennium, of all the academic papers that were cited when applying for new drug patent, only 15% were from drug company's research, 54% were from academia while rest of 13% were from research done by government agency.[35]

To sum up, brand name company has a competitive edge over generic manufacturer in its size and financial prowess. As in the case of Taxol, BMS is brought in by NCI as a commercial partner because NCI lacks the financial resources to keep up the Yew tree supply. In the case of Gleevec, Novartis can step in and ripe the benefit because a researcher simply does not have the commercial channels needed to distribute the product.

4.3 Patent is Brand Name Drug's Most Effective Defense

Patent is the first and last line of defense for drug company, patent is what enable drug company to make substantial profits.[36] By comparison, Information technology industry (IT) is another sector of business where patent plays an integral part in doing business. However, unlike in IT industry where better, faster and bigger product is being introduced in a fanatic rate and leads to the price drop. In pharmaceutical industry, the next generation of new drug will not necessarily cheaper than its first generation nor will it be substantially better. In addition, unlike consumer product that consumer is free choose other brands, in drug industry that choice is left to the doctors or pharmacists, This is particularly peculiar phenomenon in drug industry, only with the

[35] Darren E. Zinner, *Medical R&D at the Turn of the Millennium*, 5 HEALTH AFF. 202(2001).
[36] 藥品專利的雙刃劍將刺傷多少人，CRIonline 國際在線網站：http://big5.cri.cn/gate/big5/gb.cri.cn/9083/2005/11/04/762@766348.htm（最後點閱時間：2013 年 7 月 6 日）。

influx of generic drugs will the drug pricing start to drop.

As mentioned, brand name drug is no match with generic drug in a pricing battle. Consequently, market exclusivity afforded by patent is really brand name drug's only defense against generic competitors and branded drug company will go to great length to defense it.

For example: Tamoxifen, a drug used in the treatment of breast cancer, which is sold under brand name "Nolvadex" by Zeneca. In 1985, Barr Laboratories intended to market its own generic version of Tamxifen, filed an ANDA paragraph IV certification, challenged Tamoxifen's patent which is hold by Imperial Chemical. A litigation battle ensued and ended against Imperial Chemical as U.S. Federal court found Tamoxifen's patent invalid and Imperial Chemical appeals in 1992.

However, in 1993 Barr settles with Zeneca which is a former subsidiary of Imperial Chemical, as one of the terms of settlement, both parties agree to vacate the Federal court's decision of holding Tamoxifen's patent invalid, in exchange, Zeneca agrees to license Barr to market Tamoxifen while Zeneca supply Barr the drug. This agreement is a win-win situation for both Zeneca and Barr , Zeneca was able to maintain its market since both Barr's generic Tamoxifen and brand named Nolvadex were all from Zeneca. Zeneca was able to keep rest of competitors out of Tamoxifen market as long as it can keep its patent valid while Barr is allow to have a piece of Tamoxifen market provided it agree to keep others out by vacating the judgment that holds the patent invalid. Both parties were winners in this case with customer being the only loser as they still need to pay a patented drug price for a product whose patent does not warranted such protection.

4.4 Pharmaceutical Patents

There are four categories of patents for pharmaceuticals and in U.S. and its patent term lasts 20 years.

1) New Molecular Entity (NME)
2) Intended Use
3) Process and Formulation
4) Method of Administration and dosage

NME is referring to the active ingredient within a drug and intended use is referring to the illness the drug is intended to provide relief from. Process and Formulation is referring to technique and manufacturing process or methodology that involved in a drug's manufacture and formulation includes substances such as different salt, complex, enantiomer. A new combination of previously approved drug is an example that may qualify for a new patent in formulation. Method of administration and Dosage is referring to the physical appearance of a drug such as in capsule, powder or tablet etc. and how it is administrated into a patient i.e. via injection or taken orally.

Patents in pharmaceutical must satisfy the three criterions of "novelty", "non-obviousness"and "industrial usefulness" to be eligible for patent protection, just like patents in other industries with the only exception on "usefulness" criterion. A new pharmaceutical patent does need to have a readily available industrial application as long as it can helpful for future research, it will have satisfied the "industrial usefulness" requirement.

There is a disparity of jurisdiction between patent right and drug approval process. While US Patent and Trademark Office (USPTO) is responsible for reviewing for patentability but FDA is the agency that has the jurisdiction over a drug market approval. In general, a drug company will apply for patents on its NME, manufacture process or etc. as soon as possible and usually during phase 1 of clinical trial if possible. However, drug tested in phase 1 is usually years from actually enter the market if ever. As clinical trial and subsequent FDA approval will take years to complete, precious years on patent term is slipping away. Market Exclusivity is answer to such problem. Under Federal Food, Drug, and Cosmetic Act under section 505(c)(3)(E) and 505(j)(5)(F), [37] five years of market exclusivity is provided for applicant whose product is never approved by FDA before i.e. for NEM, while three years protection is available for applicant whose product is based on a known drug i.e. reference but made small modifications on them, leads to improve its performance on patients such as reduced side-effects or new intended use. The market exclusivity period is guaranteed regardless of the product's patent status when it enters the market, during this period it is free from competition of other generic and "me-too" drugs. As during this period, FDA will no review any ANDA and 505(b)(2) application, i.e. new drug application on any of the listed drugs under FDA with applicant's own modifications.

In summary, there are three potential hurdles a Generic Drug Manufacturer must pass before its drug can hit the shelf. Generic drug can't market while brand name's patent term or market exclusivity is still valid and it must not infringe reference drug's other intellectual rights such as copyright.

[37] *Small Business Assistance: Frequently Asked Questions for New Drug Product Exclusivity*, FDA, U.S. FOOD AND DRUG ADMINISTRATION (last updated June 1, 2010), http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069962.htm.

Chapter 5: Evolution Regulatory Regime

5.1 Evolution of Regulatory Regime

It is not uncommon for a drug to have multiple patents. For example, Tagamet by GSK has more than 26 patents on it. For a new drug, its active ingredient will have one patent, its manufacture process can warrant another if not more patents and a drug's delivery system or even its compound's crystal size[38] are potentially patentable as well.

Today pharmaceutical patents enjoy strong protection under U.S. regulatory regime and it has come a long way from its humble beginning in 1962. There are three important legislations that make U.S. regulatory regime what it is today. They are:

1) Federal Food, Drug and Cosmetic Act (FFDCA) in 1962
2) Drug Price Competition and Patent Restoration Act, a.k.a. Hatch-Waxman Act (HWA) in 1984
3) Medicate Prescription Drug, Improvement and Modernization Act (MMA) in 2003

Before 1962, for drug to obtain market approval, it only needs to prove it is safe to use. However, since the enactment of FFDCA, it places an additional requirement of efficacy on drug approval. The same efficacy requirement is imposed on both new drug and generic drug.

[38] *See* Bayer AG v. Elan Pharmaceutical Research Corp., 212F. 3d 1247 (Fed. Cir. 2000).

FFDCA is aimed to solve many short-comings of previous market regulations. Before FFDCA, in order to obtain market approval, applicant must conduct of pre-clinical and clinical trial to ensure its drug's safety even for generic drug whose pioneer drug may have been on the market for years. In some instances, FDA will also accept data reference or literature reference with existing drug as proof of safety; however, brand name drug's clinical data is protected by data exclusivity and gaining access to required literature is proved to be difficult for many of the generic companies as well. To worsen the situation for generic companies, conducting redundant experiments and clinical trial are time-consuming and expensive, it presents a great obstacle for generic drug maker who usually do not have the resources as most of the brand name companies do.

In *Roche Products Inc. v. Bolar Pharmaceutical*, Bolar was prevented from conducting experiments on Roche's branded drug during its patent term. Even though, the purpose of Bolar's experiments on Roche was to meet FDA's regulatory requirement on safety and efficacy.

As the result of this ruling, before the advent of Hatch-Waxman Act, there are close 150 branded drug with expired patents but with no generic drug there to compete with them.

5.2 Drug Price Competition and Patent Term Restoration Act of 1984

Drug Price Competition and Patent Term Restoration Act, also known as "Hatch-Waxman Act," (HWA) is a revolutionary piece of legislation for pharmaceutical industry. Before HWA, as demonstrated in *Roche v. Bolar*, any types of experiment or

use of branded drug during its patent term is considered as an act of infringement. Consequently, it prevents generic company from conducting experiments or clinical assessment before its patent expires. In addition, since generic drug maker can only conducting bio-equivalency test and apply FDA review after branded drug's patents expire, it effectively give brand name drug, months or even years of de facto monopoly without generic competitors due the time needed for generic company to complete these tests and procedures.

From brand name drug maker's perspective, a new drug's research and development process is risky and time consuming, they generally will apply for patents of any breakthroughs, may it be new molecular entity or new manufacturing process, discovered during clinical trials, long before the drug enters the market. While such practice protects their innovation, precious time on monopoly is wasted on clinical trial and FDA review. Consequently, branded drug may have less than half of its supposed patent term left when the drug eventually enters the market.[39]

Hatch-Waxman Act is the Congress's answer to these problems. As mentioned, for generic drug maker, not being able to conduct experiment on branded drug during its patent term give months of monopoly to brand drug by default. While for branded drug manufacturer, applying for patent as soon as possible prevent its innovation from being infringed by others but precious time afforded by patent exclusivity is lost to trials and FDA review.

HWA attempts to balance the issues and concerns from both end of spectrum

[39] Robin J. Strongin, *Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability*, NAT'L HEALTH POL'Y FORUM BACKGROUND PAPER, June 21, 2002.

through introducing several new regulatory regimes:

1) Patent Linkage system and Orange book
2) Abbreviated New Drug Application (ANDA)
3) Data Exclusivity
4) Patent Term Restoration
5) Experimental Use Exception

This fundamental purpose of Hatch-Waxman Act is "to balance conflicting policy objective: to induce brand-name pharmaceutical firms to make the investment necessary to research and develop new drug, while simultaneously enabling competitors to bring cheaper, generic copies of those drug to market." Since its enactment, the percentage of prescription for generic drug increased from less than 20% in 1984 to close to 50% in 2004 while only encompassed about 10% expense on total prescription cost.[40]

5.3 Experimental Use Exception

Previously, in *Roche Products Inc. v. Bolar Pharmaceutical*, the Court held that using active ingredient of a patented pioneer drug to meet FDA's marketing approval requirement is still an act of infringement because generic applicant is making these experiments on patented drug is ultimately for commercial purposes.

In *Roche v. Bolar*, Bolar intended to market its generic drug as soon as reference drug's patent term expired, thus Bolar conducted a serial of experiment on branded drug in order to meet FDA's requirement of bio-equivalency. A prolonged litigation battles

[40] *See supra* note 1, at 210.

ensued and ended in against Bolar in favor of Roche.

With advent of HWA, it provides an exception clause[41]. For generic drug maker, it provides that "generic manufacturer may obtained a supply of patented drug product during the life of the patent and conduct tests using that product if the purpose of those test is to submit an application to FDA for approval."[42] After HWA, generic company is able to conduct experiments and clinical research related to its ANDA application free from infringement liability.

5.4 Patent Term Restoration

One of the goals of patent exclusivity is an incentive to encourage innovator by granting market exclusivity of his innovation. In pharmaceutical research, however, due to long clinical trial and FDA review, it may take up to 8 years for an pharmaceutical innovation to actually enter the market. To remedy this problem and provide continuous incentive for new drug research, HWA allows up to five years (for NME) or 3 years for other innovation of additional patent terms for time lost during the application procedure.

Moreover, patent term extension also provides a specific incentive for drug company to engage in special research namely, research into rare disease research and pediatric research. Rare disease is categorized as an illness that has less than 200,000 patients. Since its patent population is so small, economic return for a drug

41 35 U.S.C. 271(e)(1).

42 35 U.S.C §271(e)(1) (2006). ("It shall not be an act of infringement to make, use, offer to sell, or sell within the United States . . . a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs . . . .).

manufacturer for developing drug for these illnesses is small. To remedy this situation, Orphan Drug Act was introduced in 1983 where it gives numerous incentives, most importantly 7 years market exclusivity to drug company who produce an orphan drug despite the drug's patent status. In other words, the drug company is guarantee at least 7 years of monopoly to recoup its expenses for researching an orphan drug even if such drug may involve patented innovation.

Similarly pediatric exclusivity gives drug company an additional 6 months for patent term extension, in other words, this market exclusivity is designed to recoup time drug manufacturer lost in conducting clinical trial on a drug that designed specifically for children's physiology.

Children population, similarly like patients with rare disease, are a comparatively small population compare with the general public. Moreover, drug company is difficult to obtain informed consent from children to enroll into clinical trial because children are too small to be legally eligible to make the decision on their own and it is up to the parent who will have to make the decision for them. Perhaps the greatest moral dilemma is that it is also the parents who will be getting paid. To avoid the potentially troublesome ethical issue for these types of experiments, drug company tend to avoid conducting experiment on children to avoid liability. However, children due to their unique physiology tend to response to pharmaceutical compound differently from adults. Drugs that are safe for an adult may have serious side effects on a child. Therefore, special market exclusivity is established for pharmaceuticals that offer special accommodation for children.

6 months may seems an relatively short period but for a pharmaceutical product

especially a popular one, 6 additional months of market monopoly can translates into millions even billions of profits. Drugs such as Prozac and Zoloft for instance, can bring additional 300 million in revenue in their monthly sales while for popular drug such as Prilosec, it will earn additional 1.4 billion for AstraZeneca for each additional month it maintain monopoly.[43]

While pediatric exclusivity does provide strong incentive for drug maker to conduct research specifically for children, critics are concern the exclusivity is essentially a windfall for drug company and must be limited. Amendment proposal has being raised in House of Representative to cap profits from pediatric exclusivity to 100% of pediatric research costs and a maximum 10,000% return. This proposal, however, was nevertheless defeated. [44]

Another suggestion is to give FDA the authority to require drug company to test their drugs on children. As Dr. Marcia Angell and Arnold Relman, both past editors of New England Journal of Medicine put it: " there would be nor need to offer handout to America's most profitable industry to do what they should already be doing: testing to make sure its products are safe for everyone who will use them." Their sentiment is shared but many. However, so far it is yet materialized into any real regulation.

5.5 Data Exclusivity

Data Exclusivity is meant to protect data gathered during a drug's development, as these data are proprietary to the developer i.e. usually the brand name drug company

[43] *See supra* note 9.
[44] *Id.*

and these data are protected from being cited or used as an reference by other drug developers for a period of time. Other drug developers and even the governing authority such as FDA are bound by data exclusivity during this non-disclosure period. Other drug developers who are usually generic drug makers in this case, unless being authorized by the original developer, data under drug exclusivity cannot be used as reference to prove generic drug's safety and efficacy. Such requirement as previously mentioned is the essential requirement imposed by governing agency to in order to obtain market approval. From governing agency's perspective, for any data that is still under the term of exclusivity, any new applicant who based its drug on these exclusive data will need to submit its own first hand data instead of relying previously submit data to prove application's efficacy and safety. In order to gain first hand data, applicant usually will need to conduct similar experiments and clinical trial as the first applicant. In other words, as long as the first applicant's data is still under data exclusivity, any subsequent applicant is prevent from citing the said data and will need to conduct their own experiments to gather their own data.

When a new drug is entering in a market, the drug's manufacturer will need to pass a review or registration process. During this process, manufacturer will be required to submit data on drug's active ingredient, manufacture practice, animal testing data, human trial and quality control to the regulatory agency to ensure drug's safety and efficacy. These data are both complicated and massive in volume. Consequently, in countries such as United States and Japan, specific government agency is set up to review these data as per requirement by Agreement on Trade-Related Intellectual Property Rights (the TRIPs). Under this agreement, WTO requires its member countries

to enact regulatory measurement to prevent " reliance and unfair commercial use"[45] without originator's consent to, to use data submitted during registration for the purpose of manufacturing or marketing copied drug during a period of exclusivity. However, for countries that do not have such agency in place, they usually rely on evaluation result from countries that do to decide whether a new drug will be allowed to enter their market or not. In other words, if a new drug is allow to market in countries such as United States or Japan, this drug will usually be approved to market in these countries as well.

Another potent effect of data exclusivity is its competitive edge. [46] Data exclusivity provides a powerful mean for a drug company to achieve market monopoly. During a drug's data exclusivity period, any subsequent drug makers who want to market the same drug will need to produce their own experiment and clinical data. However, conducting the same scale of experiments and clinical trial is time consuming and expensive. From a subsequent drug maker's perspective, conducting their own experiments is hardly worth the effort since term on data exclusivity is likely to over before it can finish these experiments. In other words, data exclusivity is a potent deterrent against other drug makers to market their own generic version during its exclusivity period.

Under Hatch-Waxman Act, data exclusivity runs for up to 5 years for new drug and 3 years for drug with new indication in the States.

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[45] TRIPs § 39.3.

[46] 鄭耀誠，論藥品研發、上市許可之規範與相關智慧財產權之保護－專利連結、資料專屬與專利權之探討，輔仁大學財經法律學系碩士論文，頁 25-27（2009）。

5.6 Patent Linkage and Orange Book

Patent Linkage is a new approval criterion introduced by HWA that links a generic drug application's market approval with its reference drug's patent status. Before advent of HWA, patent registration and approval are administered by United States Patent and Trademark Office (USPTO) while drug's market approval fell under the jurisdiction of Food and Drug Administration (FDA). In general, drug company will apply for patents associated with the new drug during its clinical phase. Once the said drug had obtained its patent registration number, drug company can petition FDA to list patents associated with the new drug into "Approved Drug Products in Therapeutic Equivalence Evaluation," known as "Orange Book." Patents that can be listed in Orange book are "composition" which include drug compound i.e. the active ingredient, "specific formulation" and "method of use."[47] "Orange Book provides notice to potential ANDA applicants of the patents which may protect the pioneer drug product, thus allowing them to provide appropriate certification…"[48]

Orange Book under patent linkage system will later become heated litigation battleground between generic and branded drug maker. Since FDA application review for any new drug application usually takes place years later after its patent registration and a new drug usually has multiple patens associated with it, Orange Book is an important platform for information disclosure for both generic and branded drug manufacturers. In another words, patent linkage system "links" a generic drug's market approval process with patent status of the pioneer drug in a FDA drug review procedure.

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47 21 U.S.C. § 355(b)(1)(G).

48 Abbot Laboratories v. Zenith Laboratories, Inc., 934 F. Supp. 925, 934 (N. D. I11. 1995)(quoting from FDA decision regarding Docket No. 94P-0114/CPI and PSA1, Jan. 5,1995, at 4).

While patent linkage and Orange Book are meant to protect branded name company's patent and prevent generic drug maker from unwittingly infringing other patents, it is full with loopholes that is a major subject for abuse by pioneer drug company. These abusive manipulation of systems will be disused in greater detail in later chapters.

Abbreviated New Drug Application (ANDA)

As mentioned, HAW is designed to balance the interest of fostering research for the Brand-Name company and promote prompt entrance of generic drugs into market. ANDA system is enacted to facilitate such goal.

ANDA is a streamlined market approval procedure that allows generic drug applicant to submit data or literature reference associated with its application that can demonstrate the applicant's generic drug has the same:

1) Active ingredient
2) Basic pharmacokinetics
3) Bioequivalence

As its reference drug, an ANDA applicant is allowed to use clinical data of application's reference drug as supporting data to fulfill FDA's requirements on efficacy and safety. ANDA application will receive a tentative approval, if there is no pre-existing market exclusivity in effect, the said generic drug can be marketed promptly.

There are several regulatory features that distinguish ANDA:

1) 180-days Market Exclusivity: first successfully ANDA applicant will received a 180-days market exclusivity
2) Patent Certification System
3) 45 days notification period to patentee/NDA holder[49]
4) 30 months stay period

As mentioned, one of the legislative purposes is to foster prompt generic drug's availability after branded drug's patent expires while protecting the patentee's right. Consequently, a unique regulatory framework was born. Under this new system, generic drug maker can petition for market approval without the burden of conducting redundant and expensive clinical; additionally, it is also permit to conduct experiment on branded drug a.k.a. reference drug while its patent term is still valid in order to summarily enter the market once its reference's drug patent expires.

To balance pioneer drug maker's interest, generic drug company is placed an additional regulatory obligation to check patent status of its reference drug i.e. the pioneer drug which generic drug is based on. Orange Book provides a valuable information disclosure platform for both generic and brand name drug Company, as ANDA applicant is required to check i.e. certify against the status of its reference drug's patents that were listed in Orange Book. This certification ensures generic drug that obtained market approval from FDA will not violate branded drug's patent. There are four certifications a generic drug applicant may apply to "each" patent claims associated with the reference drug that ANDA applicant wishes to copy. Generic drug applicant may assert that I) there is no patent listed under the reference drug that generic drug is

[49] 21 C.F.R. § 314.107.

based, or II) reference drug's patent has expired or III) reference drug's patent is still valid and generic drug applicant is agree to market after its patent term, during which generic applicant will only received a tentative approval from FDA, or IV) reference drug's patent is valid or will not be infringed by generic drug, this claim also known as "Paragraph IV Certification."[50]

Paragraph IV Certification

Paragraph IV Certification is a frequent point of contention between drug companies. Since a successfully paragraph IV challenge allows the challenger who is usually a generic competitor to enter the market before the pioneer drug's patent expires. In addition, the paragraph IV challenger will also entitle to enjoy a 180-days of market exclusivity. During this time FDA will not approve any subsequent ANDA filer of the same drug until 180 days after first challenger has commercially marketed its generic drug. The 180 days exclusivity is designed for the first successfully paragraph IV challenger to be the only generic drug supplier during this exclusivity period, naturally brand name company or the NDA holder will do their best to prevent it from happening or set up obstacle to discourage generic drug company from being the first challenger of their patents.

From FAD's perspective, since FDA is an administrative agency thus it does not assess the patentability and the status of patents listed in Orange Book (to be listed, drug company only need to submit a patent application number), it is difficult for FDA to ensure the patent status of its Orange Book registry. This position is also upheld by the

[50] 21 U.S.C. § 355(j)(2)(A)(vii).

court, where it states: “Orange Book listing creates no presumption that the patent is listed correctly because the FDA lacks resources and expertise to properly review submitted patents[51].” Therefore, paragraph IV certification acts as a market selection mechanism, any Orange Patent that is no longer patented or has dubious patent claims is an inviting target to be challenged by generic drug applicant.

180 days Market Exclusivity

From a generic drug applicant’s perspective, Paragraph IV Certification allows the first successfully challenger to have a 180-days market exclusivity[52] during which time FDA will not approve any other generic drug application (ANDA). The generic challenger will need to serve a notice of its claim that includes a detailed factual and legal analysis on why NDA holder’s patent is either not infringed or invalid by generic drug. The patentee of the pioneer drugs who is usually a brand name company will have 45 days to review challenger’s claims and decide whether to pursuit an infringement action against the generic applicant. 180-days market exclusivity is a lucrative incentive for generic drug maker especially if its reference drug is a blockbuster drug. 180-days market exclusivity is the reward in exchange of undertaking costs and risks of patent litigation of being the first successfully challenger of a pioneer drug’s patent. During this period of being the sole generic drug supplier, generic drug usually priced just slightly lower than the branded drug but is still significantly higher than after multiple generic suppliers have entered the market. For instance, branded Prozac priced at 2.13 USD per capsule, its first generic equivalent

[51] Ben Venue Labs., Inc. v. Novartis Pharm. Corp., 10 F. Supp. 2d 446, 456 (D.N.J. 1998).
[52] 21 U.S.C. § 355(j)(5)(B)(IV).

priced at 1.91 USD when it was first introduced. After market exclusivity, generic Prozac from various other suppliers priced at about 0.32 USD per capsule.

30-Months Stay Period

From patentee's (brand name drug) perceptive, the 45 days notice period allow them a chance to assess a generic competitor's data and decide whether to press for infringement action or not. In addition, even if patentee did not initiate any lawsuit during the 45 days period, patentee still can take an infringement action against generic drug maker after its product enters the market.

Once brand name company decides to sue for infringement against generic drug applicant, FDA will unconditionally stop its application review pending the result of the litigation as to prevent granting market approval to infringing product which may face a recall if court did find the generic drug is infringing a patent. The stay period will end when:

1) Pioneer drug's patent term expires
2) Final court decision of non-infringement for ANDA applicant
3) After 30 months[53]

During the stay period, FDA can only tentatively approve the ANDA which can be marketed immediately upon the end of stay period but is contingent upon the resolution of the dispute. While congress believes that "this procedure fairly balanced the right

[53] 21 U.S.C. § 355(j)(5)(B)(3)(1)-(4).

of a patent owner to prevent others from marketing, using, selling its patented product and the rights of third parties to contest the validity of a patent to market a product which they believed is not claimed by the patent,"[54] as in accordance with the spirit of HAW. However, 30 months stay period, for all intents and purposes, unconditionally grants brand name company, an additional 30 months to be free from generic competitors. Since usually only the first generic drug applicant will challenge brand name company's patent, 30 month stay period just give brand name drug more time on its market monopoly, for blockbuster drug, 30 months monopoly will means additional billions in profits.

In another incident, Geneva and Noropharm filed an ANDA to produce generic terazosin hydrochloride of which Abbot Laboratories is the NDA holder of its branded version. Though, its patents had already expired but Abbot Laboratories alleged its patent's filing date should count from date of divisional application rather than from date of original patent application.[55] Therefore, its patent term is still valid which allows NDA holder to raise an infringement sue against ANDA filer. Abbot's claim was summarily dismissed by district court and subsequently by federal circuit court. [56] Nevertheless, despite NDA holder's clear lack of legal basis in its claim, both of Geneva and Noropharm's ANDA were put on stay by FDA. As the result, Abbot Laboratories was able to enjoy over a year of de facto monopoly from its patent-expired drug.

In short, while 1984 HWA did help facilitate the marketing of generic drug, it is also full of potential loophole that most brand name drug will not hesitate to take

54 H.R. Rep. No. 98-857, pt. 1, at 28(1984).
55 *See* Abbott Laboratories v. Novopharm Ltd., 38 U.S.P.Q. 2d 1309 (N.D. I11. 1996).
56 *See* Abbott Laboratories v. Novopharm Ltd., 38 U.S.P.Q. 2d 1535 (Fed. Cir. 1997).

advantage of. For the next decades, pharmaceutical industry will be ravaged by litigation battles between brand name and generic drug makers.

5.7 Warring Period of Pharmaceutical Industry

ANDA and Patent Linkage system was introduced by 1984 HWA and is aiming to strike a balance of medical innovation and economic drug pricing. ANDA's patent certification system, ensure pioneer drug's patent will not be infringed by generic and provide market exclusivity as incentive for generic applicant who is willing to challenge invalid patents. Patentee's right is protected by 45 days review period on generic drug application claim which includes its confidential experiment data for patentee to assess generic drug's patentability with their own. If patentee decides to take infringement action against generic drug applicant, a 30-months stay period will be placed on an ANDA in dispute pending upon the litigation result.

While FDA's position under this regulatory regime is impartial, this system is full of potential loopholes to be exploited and abused. Some of the most common exploits included:

1) Multiple Stay Period
2) Shame Patent & Multiple Orange Book Listing
3) Reverse Payment[57]
4) Authorized Generics

[57] Sheila Kadura, *Is an Absolute Ban to Prevent Anticompetitive Agreements Between Branded- and Generic Pharmaceutical Companies?*, 86 TAXES L. REV. 647-666(2008).

These are stalling tactics commonly employed by brand name company against generic pharmaceutical firm.

5.8 Multiple Stay Periods

Stay Period is originally meant to be a period where legal disputes can be resolved before hand so that FDA can approve an generic drug that is patent-wise valid. This measurement is designed to avoid patentee from pursuing an infringement action after generic drug has entered the market for the sake of patients and healthcare providers such as hospitals and doctors. Imagine the inconvenience and disruption it will cause, if an approved generic drug is later recalled from market because of infringing a branded drug's patents.

However the catch here is: the grant of stay period is automatically and before 2000, it can be invoked on per patent basis. In other words, patentee can have multiple stay periods per each of the patents that are associated with patentee's drug listed under Orange Book. To worsen the situation, patentee is free to submit more patents into Orange Book even during the litigation proceeding against an ANDA challenger. This is exactly what happened in *SmithKline (GSK) v. Apotex*. [58] GSK (brand manufacturer and patentee) brought an infringement sue against Apotex (a generic drug company). During the litigation proceeding, GSK applied for an addition of 9 more patents into the Orange Book and sue Apotex for infringing 4 of out of its 9 newly listed patents.

By doing so, GSK had successfully re-triggering the automatic stay period against ANDA applicant i.e. Apotex. The overall stay period of Apotex as the result of these

[58] GSK v. Apotex, 439 F.3D 1312 (Fed.Cir.2005).

new patents was over five years. Brand name company can use the 30 month stay period to effectively bar its generic drug competitor from enter the market. Especially since stay period is automatically trigger by alleging a new infringement, the legality of these infringement sues are irreverent, as long as brand manufacturer is able to delay the entrance of generic, such company can cull great revenue from monopoly.

Automatically stay presents a great problem in terms of its legality. The granting 30 month stay period is, in essence, a preliminary injunction[59] against generic company with the exception of no need for the brand name company to go into trial and spare them the burden to provide any substantial evidence to the alleged infringement.

Usually, in order to obtain a preliminary injunction, the plaintiff's allegation will undergo a court's careful scrutiny. Usually a successful claimant will need to provide evidence of irreparable harm if no injunction is issued and along with proofs that show they stand a good chance to prevail in the infringement action. In a typical patent litigation, patentee will need to demonstrate: 1) a reasonable likelihood of success on the merits; 2) irreparable harm if an injunction is not granted; 3) a balance of hardship tipping in its favor; 4) injunction's favorable impact on the public interest. [60] However, in this instance, an administrative agency i.e. FDA is able to issue a ruling that ,in effect, is similar to a preliminary injunction without any legal and factual basis for doing so and provides no venue to appeal its decision.

Regarding the case, although Aptoex had already fulfilled BE requirement

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[59] Brian Range, *The ANDA Patent Certification Requirement and Thirty-Month Stay Provision: Is it Necessary* , THIRD Y. PAPER(2001) , http://dash.harvard.edu/handle/1/8852164.
[60] *See* Amozon.com v. Barnesandnoble.com, Inc., 239 F. 3d 1343 (Fed. Cir. 2001).

specified by FDA's regulation, due to patent linkage restriction, its ANDA was denied.

Multiple Stay Period strategy is only possible because patents listed in Orange Book are no monitored for its patentability nor its change in patent status once they were listed. Many patents that are later listed is not there to protect pioneer drug's innovation but as a deterrent against future generic drug applicant. Such as patents on metabolite, drug intermediate, product-by-process. This patent serves as a litigation hurdle that brand name company can throw at generic company in a dispute. While most of the time, (close to 75% from 1998 to 2001)[61] litigation will resolved in favor of generic company, it is a phyric victory nonetheless. As by the time generic drug maker prevails in litigation, the time lost during the legal battle is enough for brand name company to cull substantial profits on its legally dubious drug, and these profits is usually be far much more than the money it spends on litigation.

5.9 Sham Patent

Patent is the most effective defense of brand name drug company against competitor and thanks to patent linkage system, any generic drug that wish market a generic equivalent of pioneer drug in Orange Book and obtain market approval from FDA must first certify its patent status with patents listed in Orange Book. FDA governs Orange Book and FDA does not review patentability of listed patents. "FDA's long-standing policy of avoiding patent disputes, as evidenced by its willingness to list in the Orange Book virtually any patent submitted by an NDA holder and its refusal to hear any challenge to the adequacy and completeness of a generic applicant's Paragraph

[61] Meir Perez Pugatch, *Intellectual Property and Pharmaceutical Data Exclusivity in the Context of Innovation and Market Access* (May 15, 2009).

IV certification."[62] From a regulatory perspective, a party who is usually a generic company may dispute the legality of patents listed in Orange Book. The said party may raise its concern by stating its ground of disagreement to FDA. FDA will request the NDA holder to either amend or withdraw its patent. However, NDA holder may refuse such request and patent remains listed in Orange Book. [63] Obviously, this procedure for amending Orange Book provides very little remedy to generic company. FDA's approach plays to the advantage of brand name company who is usually a NDA holder and opens many door for legal exploits. One strategy that Brand Name company uses as a basis for triggering multiple stay periods is the so-called "sham patent." Sham patent is patent that is superficially related to the pioneer drug such as patents on metabolite, packaging feature (package insert) or intermediate etc. These patents' may or may not be patentable. However, common purpose of these patents is to provide a cause of action for infringement sue against generic drug competitors for the sole purpose of causing disruption or stalling competitor i.e. generic drug maker's business. In other words, while patents ,which is also known as AI patents,[64] on brand drug's active ingredient is justified for protection, problems arises when patents that are on ancillary aspect of a drug were entered into Orange Book for the purpose of blocking other generic competitors.

In an extreme case, a brand name company may even knowingly list a fraudulent patent into Orange Book and use it to against other generic competitors. As demonstrates in FDA's consent order[65] with Bristol-Myers Squibb (BMS) where BMS

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[62] Terry G. Mahn, *Patenting Drug Products: Anticipating Hatch-Waxman Issues During the Claims Drafting Process*, 54 Food & Drug L.J. 245, 250 (1999).
[63] 21 C.F.R. § 314.53(f).
[64] *See supra* note 30, at 3.
[65] *In the Matter of Bristol-Myers Squibb Company File Nos. 001 0221, 011 0046, and 021 0181*,

is found to fraudulently list patents associated with paclitaxel, which BSM markets under brand name Taxol, into Orange Book.

Taxol is used in treatment of ovarian cancer and paclitaxel, the active ingredient of Taxol is a naturally occurring substance and was discovered by National Cancer Institute and its information is placed in public domain that makes paclitaxel not patentable.

While active ingredient itself is not patentable, BMS is able to obtained patents on Taxol through its modification on its different methods of administration. However, BMS knew few of the studies it uses to demonstrate safety and efficacy for FDA approval were false but BMS decided to withhold this information to USPTO. In addition, BMS also deliberately fails to disclose prior art. Since BMS had obtained these patents through inequitable conduct and thus render these patents unenforceable under UPSTO ruling. BMS, nevertheless, submit these unenforceable patents to be listed in Orange Book and brought infringement sue against ANDA paragraph IV challenger based on these patents and successfully trigger 30 months stay period. In other words, BMS is able to delay ANDA paragraph IV challenger for 30 months based on fraudulent patents that it knew but listed anyway into Orange Book.

In 2000, American Bioscience, Inc. (ABI) obtains a dosage form patent on paclitaxel and sues BMS for infringement. However, this patent is based on known information from public domain source and BMS is well aware of this fact as well. Nevertheless, in order to stay off other generic competitor, BMS and ABI entered into agreement where

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ANALYSIS TO AID PUBLIC COMMENT (last visited June 6, 2013), http://www.ftc.gov/os/2003/03/bristolmyersanalysis.htm.

ABI will license its patent to BMS while enjoy a percentage of royalty based on BMS sales of Toxal which is worth over 1 billion annually in 2000. BMS subsequently submit the said patent into Orange Book. In other words, while BMS knows that ABI's patent is invalid but nonetheless submit the patent into Orange Book because BMS is able to use it as a powerful procedural delay against any other subsequent ANDA applicant.

5.10 Reverse Payment and Approval Bottleneck[66]

As evidenced from previous discussion, time is always on brand name company's side, the longer it can delay generic competitor, the better. Procedural delay and using sham patents to trigger multiple stay periods are powerful weapons. If a brand name company can tide down a Paragraph IV challenger with procedural delay until its patent term on pioneer drug expires, the ANDA applicant will be required to amend its certification from Paragraph IV to Paragraph II and will no longer be eligible for 180-days market exclusivity. However, what if a Paragraph 4 Challenger has a strong case against NDA's patent and litigation is likely to end up badly or resolved quickly, there is another tactic brand name company may consider: "Reverse Payment."

Reverse Payment[67] is often employed by brand name drug maker when generic company stands a good chance to successfully challenge its patent. Instead of fighting a legal battle with generic company, brand name company may choose to license the generic company to make the generic version of its patented drug to reduce the financial impact that may result from entrance of a generic competitor. In other incident, brand

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66 Ankur N Patel, *Delayed Access to Generic Medicine: A Comment on the Hatch-Waxman Act and the Approval Bottleneck*, 78 FORDHAM L. REV. 1077 (2009).

67 *In re* Buspirone Patent Litigation, 185 F. Supp. 2d 363, 365-67 (S.D.N.Y. 2002).

name company may simply offer the generic competitor a substantial amount of money in exchange for the generic company who had successfully obtained 180-day market exclusivity to hold off on marketing its generic drug or simply withdraw its paragraph IV application completely.

For instance, K-Dur 20, a potassium chloride supplement by Schering-Plough. K-Dur 20 is widely used in treatment of heart disease due to lack of potassium. While potassium chloride itself is not patentable, Schering-Plough has a patent on K-Dur's coating which is optimized for slow release of drug overtime to achieve better pharmaceutical efficacy.

In 1995, Upshur-Smith files an ANDA paragraph IV certification challenges Schering-Plough's patent on K-Dur 20 which will not expire until 2006. Just before going into trial on 1997, both Schering-Plough and Upshur-Smith went into a settlement where Upshur-Smith agreed to withdraw its patent claim and ANDA, in addition, Upshur-Smith also agreed not to compete with K-Dur 20 until 2001. In exchange, Schering-Plough agreed to pay Upshur-Smith over 60 million.

The legality of this kind of reverse settlements is a heatedly debated issue and not all reverse payment is per se[68] illegal. For example *In re Ciprofloxacin Hydrochloride Antitrust Litigation (In re Ciprofloxacin)*[69], this sue is a consolidated action against Bayer A.G. and its subsidiary, Bayer Corporation. Bayer is the sole patent owner and manufacturer of Ciprofloxacin which is a popular anti-biotic (patent number 4,670,444

[68] Alan Devlin, *Exclusionary Strategies in the Hatch-Waxman Context*, 2007 MICH. ST. L. REV. 631, 639-40(2007).
[69] *In re* Ciprofloxacin Hydrochloride Antitrust Litigation, 166 Supp. 2d 740(E.D.N.Y. 2001).

issued in 1987). Ciprofloxacin is a widely prescribed drug and generates revenue for over 1 billion for Bayer.[70] The consumer alleges that Bayer makes cash payment to its generic competitor Barr Laboratories to stay out of market. Such action amounts to "unreasonable restrains of trade, contrary of state antitrust and consumer laws."[71]

More specifically, Barr Laboratories challenges Bayer's '444 patent via ANDA paragraph IV certification and Bayer responses with an infringement action. The ANDA review was placed on hold at FDA. During this stay period, Bayer enters into a settlement agreement with Barr Laboratories along with other parties. In exchange for Barr Laboratories and other generic drug makers to drop their challenge against '444 patent and amend their certification to paragraph III i.e. will market generic only after '444 patent term expires, Bayer agrees to pay over 100 million in settlement.[72]

Consumer contends, by requesting Barr Laboratories and others to recognize the validity of Bayer's '444 patent, Bayer has caused injury to consumers by denying them from accessing generic Ciprofloxacin. Such action foreclosed the consumer the option of purchasing the drug at a competitive rate.

Nevertheless, the court found such action constitutes as a violation anti-trust regulation because the terms of agreement between Bayer and Barr Laboratories do not go beyond the scope of monopoly originally conferred by Bayer's patent. Barr Laboratories and other generic drug manufacturers merely agree to enter the market after Bayer's '444 patent term expires.

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[70] *Id.* at 742.
[71] *Id.* at 745.
[72] *Id.*

While settlement between drug companies may not be per se illegal, it is nevertheless a very effective tactic in insulating brand name company from competition of other generic drug competitors. In many instances, brand name company can create an indefinite procedural delay known as "approval bottleneck,"[73] where the first successful ANDA challenger makes an agreement with brand name company not to enter the market. Being the first successfully filer entitles the ANDA applicant 180 days of market exclusivity, however, if the generic filer never enters the market, the 180 days market exclusivity can never take into effect and bars other ANDA applicants from FDA review thus deny brand name company other competitors.

In the case of Tamoxifen Citrate[74], Imperial Chemical Industries (ICI) is a researching company that specializes in developing drug for breast cancer and its drug Tamoxifen's patent is approved in 1985. Subsequently, ICI authorizes its subsidiary Zeneca to market the product. In 1987, Barr Laboratories (Barr] applies for a paragraph 4 certification on Tamoxifen and ICI filled patent infringement sue.

The Court finds ICI's patent is invalid because the court finds there are data missing regarding safety and efficiency in ICI's application to United State Patent and Trademark Office (PTO).

Subsequently, ICI and Barr reach a settlement. Zeneca agrees to pay 21 million and Barr agrees to change its application from paragraph 4 to paragraph 2. Furthermore, it agrees to hold off marketing its generic drug until ICI's patent term expires.

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[73] Matthew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171, 181(2008).
[74] *In re* Tamoxifen Citrate Antitrust Litigation, 419 F.3d 370 (2nd Cir. 2006).

This sue is brought to be violating anti-trust law for avoid court judgment on patent invalidity by their settlement.

In appeal to the 2nd Circuit Court, the Court holds reverse payment as per se violations and such settlement is suspicious since brand name company is willing to pay more for settlement than winning litigation or profits can be gained when drug entering the market for the sole purpose to slow generic drug from entering the market .

However, the circuit court concludes such settlement doesn't exceed the scope of proper measure by brand name company to protect its market exclusivity. The reason as the following:

1) The settlement does not limit or bar other patented drug or generic drug from entering the market.

2) The settlement hastens the litigation to conclude that make the patent to be challengeable by other generic drug companies

3) The content of settlement does not limit competition.

Dissenting Opinion by Judge Pooler, she holds such settlement is a violation against HWA and anti-trust laws and such settlement is detrimental to public good and a burden to medical expense.

In the case of Cardizem CD[75]. Carderem Capital LP (Carderm) successfully applied for patents from US Patent and Trademark office for Cardizem CD, a drug for

[75] *In re* Cardizem CD Antirust Litigation, 332 F.3d 896 (6th Cir. 2003).

heart attack & high blood pressure. Carderm subsequently authorized Cardeizem CD's production to Hoescht Marion Roussel (HMR.) December of this same year, Andrx Pharmaceutical Inc. (Andrx) applied for paragraph 4 certification on generic version of Cardizem CD.

The next year in 1996, Caderm and HMR jointly filed for patent infringement against Andrx's certification and FDA grants a 30 months stay on Andrx's application. During the stay period, FDA has already reviewed Andrx's application and grants tentative market approval. Andrx can market the generic drug once the stay period is over. Such decision forced Caderm and Andrx into a settlement in which Andrx agree will not market any generic or bioequivalent drug pending on the decision of patent infringement sue. In exchange for this condition HMR agrees to pay 40 million to Andrx annually.

Since Andrx is the first generic drug manufacturer to obtain paragraph 4 certification, if it does not market, it will not initiate the 180 days period which subsequently bar other generic drug application from entering the market as well.

Aside from 40 million HMR pay to Andrx for not entering market, HMR further agrees to pay 1 billion if Court further finds HMR's patent is non-infringed by Andrx as settlement to Andrx.

Furthermore, 2 months after FDA approved Andrx's application, Andrx revised its formulation and re-apply for another generic drug application and successfully gain marketing approval from FDA. In the end, HMR pays 50 millions to Andrx for settlement and Andrx markets a relatively cheaper generic drug: Cartia XT.

Federal 6th Circuit Court finds agreement made between Carderm and Andrx as per se illegal because due to their agreement the 180 days exclusivity period is barred from initiating and in effect bar other generic applicant from entering. The Court finds such act as anti-competition.

Regardless which settlement methods brand name company uses, it runs counter to HWA's legislative purpose to facilitate marketing of generic drug as soon as possible. Practice of Reserve Payment is detrimental from the policy's concern, it allows drug patent that is either invalid or expired to continue to remain on the market and adversely affected the competition. According to FDA's report, close to 75% of paragraph IV challenge can prove that brand name company's patents are either invalid or not infringed by generic drug.[76]

5.11 Authorized Generics

"Authorized Generics, " also known simply as AG, is one of the last tactic a brand name company can fall on if everything else has failed to stop its generic competitor. In the event when NDA holder's patent is not strong enough to stall the litigation process and generic challenger will not accept a settlement, brand name company may instead decide to license its pioneer drug to another drug manufacturer and marketed it as the so-called "authorized generic."[77]

Legally it is nothing wrong for a brand name company to market a generic version

[76] Alden F. Abbot & Suzanne T. Michel, *The Right of Competition Policy & Intellectual Property Law: A Perspective on Settlement of Pharmaceutical Patent Litigation*, 46 IDEA 1 (2005).

[77] 孫世昌，FTC 日前公布授權學名藥策略對美國藥品市場影響之最終評估報告，Alex's Bioscience & Law Plaza 網站：http://alex19741013.pixnet.net/blog/post/8063853（最後點閱時間：2011 年 11 月 23 日）。

of its own pioneer drug and Court have determined a brand manufacturer can market its own authorized generic during the 180-days market exclusivity period. [78] Court's rationale is as such: authorized generic is approved under brand manufacture's NDA rather than an ANDA thus it's marketing is not barred by the exclusivity. However, it begs the question whether such practice will undermine market exclusivity of the first ANDA applicant who obtains FDA approval. Since the entrance of another generic competitor will significantly threat the expected profit of the first filer.

180-days market exclusivity is an incentive meant for generic manufacturer who is able to obtain FDA approval for a generic equivalent of a patented drug. However, strength of such incentive will decrease significantly if brand name company is able to dilute the exclusivity by lunching a generic drug other than its own branded drug to prevent their market share being eroded too greatly by the emergence of another competitor.

Brand name company may choose to either license its patented drug to a third party drug maker or simply market the drug itself, repackaged it and priced it just a little bit cheaper than its own pioneer drug. Authorized Generic is a powerful tactic and is not limited by first generic challenger's 180-day market exclusivity. Market Exclusivity is only applicable to other generic drug maker and is not applicable to brand name company who is the NDA holder of the pioneer drug. Consequently, since 180-days market exclusivity only bars other ANDA applicants, even when first paragraph IV challenger prevails in infringement sue against the NDA holder, it may still face market competition from authorized generics.

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[78] *See* Teva Pharm. Indus v. Crawford, 410 F.3d 51, 54 (D.C. Cir. 2005).

Using authorized generic is a win-win situation for brand name company since not only does it allows NDA holder to recovers some of its lost profits through licensing fee (if it choose to license to a third party) but it also reduced the incentive for generic drug maker to challenge its patent because the profits from market exclusivity is no longer "exclusive" due to the presence other competitors.

Interestingly, while Authorized Generic is always bad news for a generic company, it is not always so from a consumer's perspective at least in a short term. As more competitors enter the market, lower the price consumer will enjoy because it promotes competition.

In an Interim Report[79] released by Federal Trade Commission on the effects of authorized generic drug on competition in the drug market, it finds there are total of four types of agreements involving authorized generic. They are:

Type 1: Explicit commitment not to compete with an AG

Type 2: Other promises by Brand not to compete with AG on litigated product

Type 3: Brand manufacturer appoints subsequent ANDA filer as AG on litigated product

Type 4: Brand manufacturer appoints generic company as AG on another product.

5.12 Generic Drug Challenger's Dilemma

[79] Inquiries concerning this report should be direct to: Susan S. Desanti (sdesanti@ftc.gov).

In 1993, Prozac, one of the most popular drugs is running out of its patent term and many generic drug makers are eager to get their hand on. Prozac's active ingredient will run out of its patent on 1994, but brand manufacturer still have two other patents left. One will expire on 2001 and the other will expire on 2003 which are patents that cover serotonin uptake mechanism. In 1995, CEO of a generic drug company, Bruce Downey decides to challenge the 2003 patent. Challenging patents is a risky move as it is time consuming and expensive but challenge a blockbuster drug can sometimes well worth the effort since even if just go into market a couple of months ahead of other generic companies will means billions in sales volume.

While preparing to fight a legal battle in court with generic competitors, brand name company changes its Prozac from capsule to tablet and also changes its dosage regime from taken daily to taken weekly. Moreover, brand name Company even manages to cook up a new active ingredient. Old Prozac's active ingredient was composed of mixed isomers, only one of the isomers has therapeutic effect, brand name company is able separate the two and gained a patent on it as a new chemical entity. They promptly listed these new patents into Orange book.

By doing so, brand name company is able to open up another battleground. More specifically, the generic competitor's target is the old Prozac but there is little they can do legally against the "new" Prozac. Brand name company's biggest advantage in this case is its well established distribution channels, brand name company can transfer a bulk of its patient population to the new Prozac and hereby minimized the damage for losing the old Prozac. Consequently, even if generic company manages to defeat them in court, they will only be able to gain a much reduced market size. Accordingly,

Bruce Downey said their generic product is only meant to replace the old Prozac, changes in dosage regime and NME is beyond their scope to challenge. Brand name company has already persuaded many of the old Prozac users to the new one. He said: "Our originally estimated market size is about 20 billion U.S., now we are looking at about 2 billion[80] and there is little we can do about it."

In 2001, Federal District Court found brand name's patent on serotonin uptake mechanism to be invalid and generic challenger is approved to market its generic Prozac. Branded Prozac lost about 20% of original market share in two years.

In summary, Challenging brand name company's patent is a risky business even if generic challenger manages to defeat brand name's patents in court. Brand name company may still launch its own modified version to compete with generic. With its established marketing channels, the generic challenger is left with a skewed market and much less expected return.

As evidenced from previous discussion, there are many loopholes that were presented in 1984's HWA. Consequently, many of its clauses underwent amendment and many new regulatory measurements were introduced in Medical Prescription, Improvement and Modernization act in 2003.

[80] *See supra* note 11, at 248.

Chapter 6: The Medical Prescription Drug, Improvement, And Modernization Act of 2003 (MMA)

6.1 The Medical Prescription Drug, Improvement, And Modernization Act of 2003 (MMA)

"Today I called upon the brand-name industry to cease and decease from inventing new game, that they work with us to re-balance the brand name and generic systems, and that they return to scientific research they are good at and that bas being their real contribution" by Henry A. Waxman, co-author of HWA. [81]

In response to many exploits existed in 1984 Hatch-Waxman Act, Federal Trade Commission (FTC) recommends several changes to in HWA to address these problems:

1) 30-month Stay Period is now limited to once per ANDA.

2) Settlement Agreement made between Pioneer drug company and generic regarding "manufacture, sales of generic drug, or 180 days market exclusivity" is now subject to FTC and Department of Justice for review.[82]

In 2003, these recommendations were incorporated and enacted in MMA. MMA is designed to solve many of HWA's problems especially in two areas: 1) 30-month Stay Period and 2) 180-day Market Exclusivity.

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81 *See supra* note 73, at 171.

82 *See Generic Drug Entry Prior to Patent Expiration: An FTC Study*, Fed. Trade Comm'n, at 10(July 2002), http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf.

Post-MMA 30-Month Stay Period

As per FTC's recommendation, stay period is now limited to once per ANDA. In addition, to further prevent multiple stay periods, Paragraph IV challenger need only to certify patents that were already listed in Orange Book when its ANDA was filed. In other words, NDA holder can no longer keep listing additional patents at will during litigation with generic challenger. Moreover, new submission regulation is introduced that specifically excludes patents that only superficially related to pioneer drug, such as patents on metabolite, intermediate and packing feature are no longer eligible for listing in Orange Book.

Post-MMA Generic Drug Market Exclusivity

To solve the "approval bottleneck" problem i.e. first Paragraph IV challenger who is eligible for market exclusivity but never enter the market and thus its exclusivity can never take into effect and by doing so, it prevents FDA from approving other ANDA applicants. An automatically trigger mechanism and forfeiture event clauses are introduced to address ANDA applicant's laches in exercising market exclusivity.

Generic market exclusivity now can be triggered by:

1) Commercial marketing of first ANDA applicant's generic drug
2) Commercial marketing of authorized generic by first ANDA applicant
3) By a court decision holding the patent that certification bases on it either invalid or not infringed.

Forfeiture Events

1) Failure to market

Generic challenger will forfeiture its market exclusivity if it fails to market the generic version of the patented by the later of:

aa) The earlier of the date that is:

AA) 75 days after the approval of the application of first applicant

BB) 30months after application submission

bb) With respect to first applicant (or any other applicant that has received "tentative approval"), 75 days after a lawfully maintained certification that is qualified for 180-days exclusivity, and at least one of the following occurred:

AA) an Infringement action brought against that applicant with respect to the patent or in a declaratory judgment, a court enters a final judgment from which with no appeal has been or can be taken that the patent is invalid or not infringed.

BB) In an infringement action or declaratory judgment described in (AA), a court signs a settlement order or consent decrees that enter a final judgment that include finding that patent is invalid or not infringed.

CC) Patent information is withdrawn by the holder

Other Forfeiture Events

First generic challenger will lose its exclusivity if:

1) First ANDA applicant withdraw its application

2) First ANDA applicant amend its paragraph IV certification to other certification

3) First ANDA applicant fails to obtain tentative approval within 30 months of its initial filing

4) First ANDA enters into a settlement with NDA/Patent holder or other generic drug manufacturers and terms of the agreement is found to be violating anti-trust law either by FTC or a Court.

5) All patents related to first ANDA applicant's paragraph IV certification have expired.[83]

Once the first applicant forfeits the market exclusivity, any subsequent ANDA filer that had obtained tentative approval will be approved immediately but will not have market exclusivity.

The forfeiture event is government's answer to address the problem where the first ANDA challenger does not market its drug promptly and tied FDA's hand in approving later applicants.

MMA on Reverse Settlement

Also, due to the dubious nature of settlement made between drug manufacturers, these agreements are now subject to governmental scrutiny for possible anti-trust violation. More specifically, settlement terms made between drug companies regarding

[83] 21 U.S.C. § 355(j)(5)(D).

sales and manufacturing or related to 180-day market exclusivity, ANDA applicant is required to submit terms of agreement to the supervision of FTC and Department of Justice for review of its legality.

Remedy for Orange Book Abuse

As discussed previously, many patents that were listed in Orange Book are a competition tool for the specific purpose of providing grounds for stalling future competitors with infringement litigation.

MMA's solution to this problem is in two folds: 1) Firstly, commonly known superfluous patents were specifically excluded from being eligible for Orange Book registration. For example, patents on metabolites, packing features, reaction intermediate and etc. are no longer eligible for listing. 2) Secondly, no longer always remain in passive, ANDA applicant when being sued by NDA holder for infringement in a Paragraph IV certification, is now able to bring a counterclaim of its own to delist NDA holder's patent from Orange Book.[84] If NDA holder's patent is later found the Court to be invalid or not related to listed drug, the ANDA applicant may amend its certification to Paragraph I and avoid litigation with the NDA holder.

Before MMA, even though ANDA applicant who filed for Paragraph IV certification is required to serve a notice to NDA holder of the listed drug, the NDA holder, however, is not required to response such notice within the 45 days. In other words, even if the NDA holder does not bring an infringement action against ANDA applicant during its FDA review, such patentee is still free bring the sue against generic

[84] 21 U.S.C. § 355(j)(5)(C)(II).

manufacturer even after its product has entered the market. This situation is detrimental to both public and ANDA applicant. It adds great degree of uncertainty to the medical supply system as even an approved FDA product may face a recall, shall the NDA holder decide to bring an action against the generic and also puts generic manufacturer is at a disadvantage of having to constantly worry about its product's legality and such worry may use to the advantage of a brand name company to coerce a generic company into a unfavorable agreement.

With the advent of MMA, during a paragraph IV certification process, an ANDA applicant may also seek a declaratory judgment from court for patents in question that are either invalid or not infringed by ANDA applicant's generic drug. In exchange to obtain patent certainly, ANDA applicant must grant confidential access of its ANDA application to NDA holder to determine its patentability with NDA holder's own patent.

6.2 Impact of MMA, Its Success and Failure

The 2003 Medicare Modernization Act strives to address many exploits and loopholes that existed as the result from more than a decade of HWA implementation. While it had effectively remedied some of abuses but in some instances the new provisions remains ineffective and opens a new ground for manipulation and points of contention within pharmaceutical industry.

MMA on 30 Month Stay Period

MMA succeed in eliminating multiple stay period abuse. The new MMA provision only allows one stay period per ANDA application and applicant only need to provide

certification on patents listed in Orange Book at the time of its filing. MMA provision effectively deny NDA holder to trigger multiple stay period by keep listing new patents into Orange Book as the response to ANDA applicant's paragraph IV challenge.

While it is an effective amendment; however, one issue remains: the duration of stay period is arbitrary, on average, a typical ANDA takes about 25.5 months to obtained market approval thus there are several months when ANDA applicant is sitting idle, waiting for the stay period to expire while brand name company continue to ripe the profits of its monopoly. During the drafting of HWA, the original proposed stay period was only 18 months, it was due to vigorous lobbying of pharmaceutical industry was it eventually extended to 30 months.[85] The additional months where generic drug is kept of out market is not only detrimental to general public as it helps maintain monopoly of brand name company and keep drug's pricing up, it can also potentially be disastrous to ANDA applicant in the event when NDA holder's patent is nearing its expiration.

In a scenario when a reference drug's patent has only less than 30 month of patent term remains, say a Paragraph IV ANDA applicant is able to obtained a tentative approved within 18 months but it was prevented to resume its FDA review process due to the 30 months period and reference drug's patent expires during the stay period. The said ANDA, after its stay period, will have to amend its certification from Paragraph IV certification to Paragraph I due to the patent of the reference drug it was based had expired. Amending to a different certification will mean that the ANDA applicant will

[85] Gerald J. Mossinghoff, *Overview of Hatch-Waxman Act and Its impact on Drug Development Process*, 54 FOOD & DRUG L. J. 187, 190 (1990).

not longer be eligible to receive 180-day market exclusivity. Consequently, from a generic challenger's perspective challenging a patent nearing its expiration is risky and may not worth the investment as even if it is likely to prevail in litigation with NDA holder, it may not be able to obtain market exclusivity.

MMA on Reverse Settlement

MMA attempts to address this problem with dual mechanisms, each with its own monitoring agency. MMA wish to prevent unreasonable delay of ANDA applicant with a forfeiture event clause where it states the first ANDA applicant will lose its market exclusivity if it does not promptly enter the market after receiving an approval, more specifically "75 day after the date on which the approval of the application of the first applicant is made effective." Technically, with new "forfeiture event" when first ANDA applicant does not to market within 75 days after obtaining market approval, the said applicant will lose its market exclusivity and FDA is free to approve any other subsequent applicant that had obtained tentative approval for immediate marketing.

Nevertheless, with a more scrutiny on " Failure to Market" provision, it requires to a comparison of two conditions and determine the one that is "later of" the other one to determine when the provision will come into effect.

Generic challenger will forfeit its market exclusivity if it fails to market the generic version of the patented by the later of:

aa) The earlier of the date that is:

AA) 75 days after the approval of the application of first applicant

BB) 30months after application submission

bb) With respect to first applicant (or any other applicant that has received "tentative approval"), 75 days after a lawfully maintained certification that is qualified for 180-days exclusivity, and at least one of the following occurred:

AA) an Infringement action brought against that applicant with respect to the patent Or in a declaratory judgment, a court enters a final judgment from which with no appeal has been or can be taken that the patent is invalid or not infringed.

BB) In an infringement action or declaratory judgment described in (AA), a court signs a settlement order or consent decrees that enter a final judgment that include finding that patent is invalid or not infringed.

CC) Patent information is withdrawn by the holder

Interpreting from legelation's language, FDA will need to compare the date from two conditions: (aa) and (bb) and determine which one is the later date. In a typical reverse settlement scenario where first ANDA applicant who had obtained tentative market approval from FDA and this will be governed by conditions under (aa) i.e. trigger the counting of 75 days. However, according to the legislation, condition under (aa) alone isn't sufficient to trigger the "failure to market", FDA will also need to determine the date stipulates under (bb) to determine which one is the "later of." However, the catch here is: while date stipulates under (aa) will certainly come to pass but date under (bb) will not necessarily happen in every reverse payment scenario. In the event where NDA holder never institutes an infringement action against ANDA applicant nor does ANDA applicant seeks a declaratory judgment from court, the (bb) condition will never happen. However, without (bb) FDA will not be able to compare

which one is the later with (aa). In other words, FDA interprets "Failure to Market" provision as such:

"We find under the plain language of the statue, 180-day exclusivity is not forfeited for failure to market when an event under subpart (aa) has occurred but – as in this case – none of the events in subpart (bb) has occurred. The "failure to market" provision results in forfeiture when there are two dates on basis of which FDA may identify the "later" event as described in section 505 (j)(5)(D)(i)(1). The provision does not effect a forfeiture when an event subpart (aa) has occurred but no even under subpart (bb) has yet occurred."[86]

Essentially, what FDA is saying that without event stipulate under (bb) ever occurring, the required comparison of which is "later of" will not be met. As the result, the forfeiture event will not come in effect since its legal equation is incomplete.

The ramification of FDD's interpretation will put subsequent ANDA filer in an unfavorable situation. While any subsequent ANDA filer is free to bring its own legal action against NDA holder's patent and thereby trigging condition under (bb)(AA) where NDA holder's patent is found to be invalid. However, the incentive to subsequent ANDA filer is very limited. Hatch-Waxman act encourage ANDA filer to challenge NDA holder's patent by providing 180-day market exclusivity. However, such benefits is only limited to first filer. In other words, as a subsequent filer who challenges the NDA holder, for such challenger, not only it will spend considerable resources on legal battle but it will not be eligible to receive market exclusivity even if such exclusivity

[86] *See supra* note 73, at 171-201 (2008).

was forfeited by the first filer.

6.3 Chink[87] in the Forfeiture Event Provisions

As mentioned early, in typical pay-for-delay scenario where first generic challenger agrees to stay off market for a certain time in exchange to money compensation from brand name company and such agreement will not involve a finding regards to NDA holder's patent status i.e. whether it is invalid or not infringed by the first filer. Since legal equation for failure to market required a comparison of the later of between (aa) and (bb), without an infringement sue or declaratory judgment, the event in (bb) will never occur and so does the forfeiture event.

The situation is further complicated by the fact that only the first ANDA applicant is eligible to receive 180-day market exclusivity. Even if the first applicant withdraw its application, subsequent filer still will not be eligible for the exclusivity.

Moreover, the MMA amendment also fails to address the bottleneck effect resulted from on-going litigation battle between generic and brand name manufacturers.

The forfeiture event was designed to push the approval procedure along despite the conflict between brand name and generic companies; it was designed to achieve this by placing time limits on ANDA applicant to market its product promptly after the resolution of its litigation with NDA holder. The provision (bb)(AA) reads that first applicant will lose its market exclusivity 75 days after a court decision that finds NDA

[87] *FDA's Exclusivity Forfeiture Saga continues*, IP LAW360 (last visited at June 12, 2013), http://www.avhlaw.com/media/article/111_ForfeitureSaga.pdf.

holder's patent is either invalid or not infringed. However, the catch is here that such decision is a "final judgment from which with no appeal has been or can be taken." In other words, a district court ruling will not be sufficed; at least a circuit court decision is required to trigger this condition. However, reaching a circuit court decision is a long journey that is not only a burden financially but also time consuming and as had discussed previously, in the race of drug marketing, time is essential and any delay is a victory for brand name company.

Ironically, MMA is meant to provide a remedy that allows timely influx of generic drug into market; however, requiring a final court decision in order to trigger the forfeiture event simply will not achieve such purpose. As in actual practice, it is not unusual for a case to takes years to resolve in district court let alone in circuit court. This provision is simply ineffective in dissolving issue of stalling litigation or the "bottleneck" effect.

MMA on Authorized Generic

As discussed early, authorized generic (hereinafter as AG) released by brand name company or via a third party. Even though use of AG is dubious competition-wise as such practice effectively dilutes the expected profits of first generic challenger's market exclusivity but it is in no way illegal nor is it necessarily detrimental to general consumers since with more competitors on the market, the drug pricing will tend to be lower than with only a few competitors.

However, neither HWA, nor MMA offer any solution on this issue. In the past, two prominent U.S. generic manufacturers, Mylan Pharmaceutical and Teva Pharmaceutical

filed a petition to FDA, arguing that authorized generics should treat as the same as other "generic drug" when applying for market approval thus first ANDA applicant's market exclusivity should be applicable to it as well. Nevertheless, their petition was summarily denied by FDA.

FDA alleged: "[it] does not regulate drug price and have no legal basis to prevent innovator company from marketing approved NDA products." Its decision was upheld in both 4th Circuit and D.C. Circuit Court. Court's main rationale for reaching this decision is that: while such practice will negatively affect incentive of a generic company to challenge patent but it help general public to have a cheaper pricing drug and aren't necessary "predatory or anticompetitive."

Judging from the number, authorized generic is a mixed blessing and does provide consumer with more favorable pricing. On average, when an authorized generic enters the market during first filer's 180-day market exclusivity, such an additional competitor will lower first generic drug's retail price about 4.2% and its wholesale price about 6.5%. Consequently, the expected revenue of first filer typically drops ration is between 47% to 51% from its expected revenue due to increased competition from additional competitors. While, consumer may ripe the benefits of lower drug pricing in the short term, due to severely reduced expected return, first ANDA filer may more likely to settle with brand name company which allows them to more easily consolidate its market monopoly and undermine the overall policy for prompt generic drug entrance into the market.

According to FDA report, [88] from year 2004 to 2008, there are total of 38 pharmaceutical settlement involving AG. About twenty (20) of them, brand name company settled with first generic filer, not to market their AG; however, instead of fist filer market its own generic drug, brand name company grants first filer exclusive license to market a generic version of pioneer drug supplied by brand name. In ten (10) of them, brand name promises no to launch its AG, for a period of time in exchange for generic company for forfeit its market exclusivity. In the other situations, brand name may choose to appoint subsequent ANDA filer as the producer for its AG or brand name may simply offer the first filer as the exclusive AG distributor of another drug in exchange for the generic company to forfeit its market exclusivity.

As evident from previous example, AG is a versatile weapon for brand name company. On one hand, AG allows brand name company to recoup some lost due to entrance of a generic competitor. On the other hand, AG is also a powerful coercive tool into striking a deal with first ANDA filer. It is an effective leverage that brand manufacturer can use when try to persuade generic company from stay off the market through complicated licensing agreements, this can be a potentially win-win situation for pharmaceutical companies. Brand manufacturer got to keep its market share while generic company is allow to have a piece of the action too under the exclusive licensing agreement, instead of going into cut-throat pricing battle. However, such practice undermines the originally intended purpose of market exclusivity system which was meant as an incentive for first ANDA filer to launch its own generic products to compete with brand name company.

[88] FDA Interim Report: Inquiries concerning this report should be direct to: Susan S. Desanti (sdesanti@ftc.gov).

6.4 Me-too Drug

Me-too drug is defined as a drug that is structurally similar to ones already on the market, usually based on blockbuster drug such as Liptor due to the sheer market size blockbuster drug has. Usually Me-too drug differs from pioneer drug with some modifications, such as Prilosec and Nexium. Prilosec's active ingredient is omeprazole; while, Nexium's active ingredient is esomeprazole, which is essentially the left-handed version of omeprazole.[89] Drug maker will undoubtedly market the new drug as better than its previous generation, it is certainly true in some instances, such as Troglitazone, which is marketed as anti-diabetic drug in 1997, but was soon withdrawn from market due to its high hepato-toxicity. Its successors: Rosiglitazone and Pioglitazone remedy the problem and are widely used today. However, not all "me-too" drug can boast such claim.

As mentioned, drug company will do their best to extend patent term on its product for as long as possible. Even when its drug's patent term eventually expires, drug company will often have a contingency plan in place to keep their existing customers i.e. patients to be continuingly relied on its drugs. AstraZeneca's Prilosec is one of such example. Prilosec, advertised as "the purple pill" is mainly used in the treatment of heartburn with its patent expires in 2001. Knowing Prilosec is heading to its eventual demise and its market share being devoured by generics. To prevent such fate, AstraZeneca spends millions in advertising Nexium, destined successor of Prilosec, calling Nexium: "Today's Purple Pill."

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[89] *"Me-too" Drugs: Good or Bad?*, ARTICLESBASE (Mar. 1, 2008), http://www.articlesbase.com/medicine-articles/metoo-drugs-good-or-bad-346872.html.

Nexium is a chemical variant of Prilosec and have a little improved in performance than Prilosec but not in the treatment of heartburn which is the chief intended use of the drug. Nexium's marked improvement is in the treatment of erosive esophagitis which occurs when acid from stomach backtracks and causes inflammation, swelling, or irritation of esophagus. Essentially, Nexium is a me-too drug of pioneer drug Prilosec. However, due to its slight improvement, AstraZeneca with its already established channels and marketing prowess is able stay off generic drug challengers. After a year since Nexium's debut, it is able to capture 19% of market share while Prilosec drops from 49% to 25%, in other words, AstraZeneca is able to maintain a dominate market presence of 44% even after patent expiration. As evident from these numbers, me-too drug is able to re-capture a significant market share lost by expired pioneer drug.

In most of the cases, me-too drug only offer marginal improvement at best from its predecessor. While me-too drugs usually priced lower than pioneer drug but they still costs higher than its generic counterpart. Me-too drug is motivated mostly by commercial consideration, or to prolong life cycle of a drug company's blockbuster drug. A me-too drug, in a sense, is a mixed blessing for the public. On one hand, it provides useful improvement from their previous generation or explores more possibility for a known drug class such as Statin which was originally mainly prescripts as an anti-cholesterol agent but thanks to research done in its me-too drugs, Statin-class is later found to be highly effective in preventing death from heart stork as well. On the other hand, me-too drug provides an excellent marketing excuse for drug maker to market a therapeutically almost identical drug but with a more expensive price tag.

There are several factors for "me-too" drug to be successful. 1) Market Size 2)

consumer base. As mentioned, market size is paramount consideration when marketing a me-too drug. Therefore, most of the me-too drugs are for chronic illness or lifestyle drug. Chronic illnesses such as arthritis, depression or high cholesterol have very low possibility to be truly "cured" so to speak; therefore, for most of these patients, they will be on medication for life which business-wise is a long-lasting market. Lifestyle drugs refers to drug that are used to improve patients' life quality, such as Viagra, famous drug for erectile dysfunction, which like chronic illness, it is not an immediate life threating illness but require patient to take it on regular basis. Secondly, most of me-too drug are for chronically illness, few are for acute infectious diseases such as schistosomiasis, despite these diseases' huge patient population in developing countries, few drug makers are interested in researching such drug for a simple reason: patients are simply too poor to pay for them since most population who are most vulnerable to infectious disease are also tend to be people from poor countries.

6.5 You-go-I-go tactics

Among all other tactics used by brand name, "voluntarily delisting its own patent from Orange Book," is the last resort a brand name company can use when facing competition from generic company. Unlike AG where brand Name company can use it as leverage when negotiating a compromise with generic company where a potentially beneficial arrangement can be reached by both parties, delisting its patent is more as a deterrent or as an act out of spite than a negotiation tool. By delisting its patent from Orange Book before ANDA applicant can obtain a tentative approval from FDA, once the patent is gone, ANDA applicant will need to amend its application to other certification and thus lose its eligibility for market exclusivity as it is only available to

Paragraph IV certification. Moreover, with advent of MMA, delisting is also a forfeiture event which requires an approved ANDA applicant to launch its drug within 75 days after delisting. Ironically, what was originally meant to ensure brand name company will not interfere with generic company's marketing procedure, now puts generic company an even more disadvantageous situation.

Such practice, however, does not go unchallenged. In R*anbaxy Laboratories v. Leavitt (2006)*[90], D.C. Circuit Court held that FDA may not delist a patent from Orange Book at NDA holder's request after a Paragraph IV certification had been submitted against that patent. In contrast, Cobalt Pharmaceutical filed a Paragraph IV certification for Bayer's Precose (a treatment for diabetes) listed in Orange Book. However, before Cobalt can obtain a final approval for its ANDA from FDA, Bayer requests FDA to delist its patent from Orange Book registration. Consequently, Cobalt filed a petition to FDA, requesting other subsequent ANDAs not to be approved until Cobalt's market exclusivity has run. Nevertheless, FDA rejects Cobalt's petition and found that Cobalt's exclusivity had forfeited due to Bayer's delisting of its own patent. Furthermore, FDA refuses to adopt *Ranbaxy* decision, its reasoning was that D.C. Circuit Court's decision was only applicable to pre-MMA situation.

However, the wind changed in 2010. In *Teva Pharmaceutical USA, Inc. v. Sebelius,*[91] D.C. Circuit Court held that FDA's "plain language" approach of statutory interpretation on forfeiture event is erroneous. The court condemn allow brand name company to voluntarily delisting patents from Orange Book is "diminish the incentive

[90] Ranbaxy Labs. Ltd. V. Leavitt, 469F. 3d 120 (D.C. Cir. 2006).
[91] Teva Pharms. USA, Inc. v. Sebelius, 595 F.3d 1303 (D.C. Cir. 2010).

for a manufacturer of generic drugs to challenge a patent … in the hope of bringing to market a generic competitor for an approved drug without waiting for the patent to expire."

6.6 Chapter Summary

There is little doubt that many brand name company are wealthy and powerful multinational conglomerates that enjoy strong tide with both politicians and medical academia, they are so powerful to a point that can even exert pressure to other countries via free trade agreement with U.S. either through U.S. trade representative or via entity such as PhRMA[92] into playing their games of intellectual property manipulations. This paper will elaborate more on the following chapters.

For any local generic company to have a fighting chance, a comprehensive and fore-sighting regulatory framework and an ever vigilant and impartial governing agency are essential. Hopefully, discussion and regulatory scheme's evolution presented in previous chapter will serve as a history lesson to be learnt from for Taiwan.

[92] PhRMA is an acronym for The Pharmaceutical Research and Manufacturers of America.

Chapter 7: International Regulation on Patent Linkage

7.1 International Regulations on Patent Linkage

Linkage provision requirement has being incorporated in many free trade agreement made between U.S. and many other countries. Such as Korea-US Free Trade Agreement (KORUSFTA), [93] similar agreements also exist between Canada and Australia where incorporation of patent linkage system is required as part of the free trade agreement.

An extensive survey conducted by US Federal Trade Commission (FTC) in 2002 shown as many as 75% of drug application by generic drug manufacturer is facing patent infringement action from brand name manufacturer.

Canadian System

Canada is brought into patent linkage system by 1993 North American Free Trade Agreement (NAFTA) which imposed Canadian government, more specifically Health Canada an obligation to withhold market permit to Generic Drug Company until all relevant patent of the brand name drug that the generic drug is based on have expired.

In Canadian system, when a generic company submits a generic drug application, it also will need to serve a "Notice of Allegation (NOA)" to the patent holder. The patent holder has 45 days to formulate a response to NOA. If the patent status of the

[93] Thomas A Faunce & Joel Lexchin, *Linkage pharmaceutical evergreening in Canada and Australia*, AUSTL. & N.Z. HEALTH POL'Y, June 1, 2007, at 6.

generic drug is in dispute, the patent holder can initiate an application to Federal Court of Canada, to prevent Minister of Health from issuing Notice of Compliance (NOC) to generic company. The stay period for the generic company's application is 24 months or upon the resolution of the court, whichever is sooner.

In Canadian system, a patent registry is administered by Office of Patented Medicines and Liaison under Ministry of Health, this registry is consisted of patents related or in association with drugs that have received NOC. Minister of Health may refuse to add or remove information from patent registry. In addition, each patent is independently review by the office for its patentability. Office of Patented Medicine and Liaison also produce static report on its patent registry, including information such as number of patent filed, numbers of acceptance, rejections and litigation result from accepted or rejected patented.

Overall, Canadian drug marketing procedure and patent linkage is governed by "Patented Medicines (Notice of Compliance) Regulation" also known as PM(NOC) Regulation. Its legislative structure is similar to American in many aspects. It features a pharmaceutical patent registry (much like Orange Book under FDA) and an automatic stay period on application approval if an infringement action is brought. However, unlike its U.S. counterpart, even under the new patent linkage regime, generic company still stands a better chance of winning in a litigation battle against brand name company, partially due to fact that generic drug manufacturers represent the majority of Canadian pharmaceutical industry. More overall, in the light of the 180-day market exclusivity that has caused such havoc in U.S. system i.e. brand name company upset the balance of market and reduce the incentive for the first ANDA applicant by introducing their own

version of generic drug or authorized generic, market exclusivity is not available in Canadian system. More specifically Canadian regulatory system is composed of following major elements: " New Drug Submission," "Generic Drug Submission," "45 days Notice Period," "24 Months Stay Period" and "Damage Estimation."

New Drug Submission

Canadian system limits person who file for a new drug submission must be "owner of the patent or has an exclusive license to the patent, or has obtained the consent of the owner of the patent." In addition, only four types of pharmaceutical patents are eligible for submission, there are medicinal ingredient, formulation, dosage form and use of the medicinal ingredients. Subsequently, any change to the patents listed is also limited to these four types.

Generic Drug Submission and 45 Day Notice Period

Generic drug manufacturer may file for an "Abbreviated New Drug Submission" (ANDS) with the authority coupled with a certification regarding the innovator medicine the generic drug is based on. The certifications can be of the following:

Generic applicant agree not receive NOC until the innovator medicine's patent has expired or generic applicant may allege:

1) Filer for the New Drug Submission is not eligible under PM (NOC) §4(4)(d). For example, the filer is not the patentee or is not being properly licensed by the patentee.

2) Innovator's patent is invalid.

3) Patent has expired.

4) Patent is not infringed by the generic product.

The generic company's certification or notice of allegation will need to serve to the patentee who is usually a brand name drug company within 45 days. Generic company's notice of allegation will need to contain a description of its own patent in any of the four categories: medicinal ingredient, formulation, dosage form and use of the medicinal ingredients and legal or factual basis for the allegation. Brand name company has 45 days to response once it has received notice of allegation. Unlike in U.S. system, brand name Company may sue for infringement directly against generic Company, under the Canadian, if brand name company found the allegation to be false, it can only seek a court order to stop the authority from issuing NOC to the generic company but cannot directly sue the alleged infringer. While during this action, generic company will still bear the burden of proof to submit relevant evidence on behalf of the authority to the court.

24-Month Stay Period

Once the action is brought, generic drug's market approval procedure will on halt for 24 months, during this time no NOC will be issued. However, Canadian system is unique in the aspect of the court may shorten or extend the time limit depending on whether both parties are cooperative in expediting application.

Damage Estimation

Damage estimation is another unique aspect of Canadian system that distinguishes itself from U.S. If brand name company withdrew, discontinued its action or action

was dismissed by the court, or if brand name company's action had prevent authority from issuing a NOC but the decision is reversed on appeal: under such conditions, the brand name company will be liable for damage suffered by Generic Company during this period i.e. time between NOC would have been issued if without interference and the time it is actually issued or time of withdrawal, the discontinuance, the dismissal or the reversal.

As evident by her regulatory measurement, Canada is trying her best to contend possible abuse that may result from incorporating patent linkage system. Nevertheless, linkage system or more specifically the threat of patent evergreen remains a matter of much heated debate in Canada. The Canadian Pharmaceutical Association (CPhA) called it " not only is this abuse of Canada's patent regime extremely harmful to Canada's generic pharmaceutical industry, the Canadian public lose out millions of dollars in saving by having to pay for the higher-priced brand name version for an extended period of time. The delays caused by these needless court battles have cost Canadian, their governments and private insurers hundreds of millions of dollars."

Counter to CPhA, Canada's own research-based company claims that " generics do not have concern themselves with possible interlocutory injunction to prevent infringing sales once an infringing product is on the market … as a result of the inability of a pharmaceutical patentee to obtain interlocutory injunction to prevent complete destruction of their intellectual property and market share, the linkage regulations are the only mean for Canada to meet its international obligation to provide an effective enforcement mechanism for patents."

As similar in the U.S., CPhA claims that brand name company delay the entrance

of generic drug into the market by continually listing new patents on existing product, each new entry will trigger a NOA and cause significant delay. Brand name company rebut such allegation by asserting new patent is only natural as it reflects the drug's improvement and it is relatively common a single drug to have multiple patents. As estimated by Office of Patented Medicines and Liaison, 44% of 419 medicines listed in Patent Registry have more than one patent.

However, the fact is not as benign as brand name company claims to be. Many new formulation of existing drug is launch for the specific purpose to switch doctors to the new drug before the generic hits the market to prevent generic from eroding its market share. For example, Torcetrapib, a drug from Pifer to increasing lipid-removing cholesterol (HDL) and is introduced into the market in combination form with Lipitor, one of Pfizer's blockbuster drug that mainly prescribes to lower low density Cholesterol (LDL). The main motivation for this combination is because Lipitor's patent will expire in 2010. This new combination allows Pfizer to effectively extend Lipitor's term since new combination of drug is eligible for new patent. However, this new combination of drugs presents many problems for patients, some patients may not be able to afford Lipitor but without Lipotr, Torcetrapib will be unavailable to them. Similarly, for doctors who only wish to raise a patient's HDL but do not want to lower their LDL, such combination of drug will prevent them from doing so, because access to Torcetrapid is tied with Lipitor. It is only when clinical trial shows that patient who take the drug in its combination form have an increased risk for cardiovascular mortality did Pfizer agree to sell Torcetrapid on its own. This kind of practice does not go unnoticed by Canadian authority; in 2006 Canadian federal government amends its drug approval process so that no new patent is allowed to file by patent holder once the

generic company has submitted an application for NOC approval. Moreover the amendment also specially excludes patent that has not direct therapeutic application such as intermediate, metabolite to be eligible for patent registry. Supreme Court of Canada also recognized the problem of brand name company abusing NOC regulation by claiming irreverent patents for the specific intention to delay entrance of generic drug into the market. Many of these patents include minor modification in drug's delivery system, formulation, and combinations.

In summary, the essence of linkage system in Canada is the same as US's Waxman-Hatch regulation that requires generic drug manufacturer to notify brand name company of its intention to enter the market. Moreover it also places additional obligations to government agency to link marketing approval of a generic drug to absence or resolution of patent claims.

7.2 Australia and The Australia-United States Free Trade Agreement (AUSFTA)

Canada is not the only country that has to set up a linkage system as a condition for free trade agreement with the US. Australia is another country that shares the similar fate. Australia's drug approval regulations differ from its North American counterparts in several aspects. Firstly, there is no specific procedure for generic drug such as Canada's ANDS or America's ANDA. It only has different data submission criterions between Generic and Brand Name products. Secondly, there is no pharmaceutical patent registry available for applicant to check each pharmaceutical product's patent status. Therapeutic Good Administration (TGA), the authority over pharmaceutical product market approval, only requires evidence of safety and efficacy of a product during its registration. Australia's approach toward a product's patent status is more loosely

controlled than Canada's. When a pharmaceutical product is applying for market approval, the applicant needs to provide a certificate made in good faith that function both as a non-infringement certification and a notice to patentee. Applicant risks penalty and punitive damage claim from attorney-general if certification is later found to be false or misleading.

Before the free trade agreement, in the case of Aktiebolaget Hassle v. Alphapharm Pty Limited[94] which is a case over a pharmaceutical patent on an oral drug with active ingredient of omeprazole in forms of tablet, capsule or pellet. In 1998, as the patent terms was nearing its expiration, Alphapharm, a generic company commerce steped in importing and selling drug with omeprazole to treat gastrointestinal disease in Australia. In August of the same year, Astra group, the brand name company, pressed an action in Federal court to restrain infringement against its patent. In this case, Justice Kirby stated in the judgment:

" The strategies that large pharmaceutical manufacturer have employed to avoid such generic competition which include use of intellectual property law, have been detail elsewhere … this Court should avoid creating fail-safe opportunities for unwarranted extension of monopoly protection that are not clearly sustained by law."

As evident by Justice Kirby's statement, brand name company trying to extend its patent term through means of manipulating intellectual property law is no stranger to Australian court even before its incorporation of free trade agreement with US. In 2004, the legal scene is becoming even more complicated with advent of Australia-US Free

[94] Aktiebolaget Hassle v. Alphapharm Pty Limited , 2002 HCA 59 (12 December 2002); BC200207518.

Trade Agreement (AUSFTA). More specifically one of its provisions has generated some very heated debate as many believe if incorporated into Australia's current legal regime will lead to inappropriate patent term extension, also known as "linkage evergreening."

Article 17. 10. 4 of AUSFTA require Australia's Therapeutic Good Administration (TGA) to formulate as legal process in which brand name company will be informed when a generic product that is based on its brand name product is filing for market approval with TGA and provides a measure in its approval process to prevent generic product form entering the market if its brand name counterpart's patent is not yet expired.

More specifically, article 17.10.4 stipulates when a party apply for marketing approval of a pharmaceutical product must provide information on product's safety and efficacy. If information submitted by the party is not of the original such as relying evidence or citation of the product that was previously approved in another countries.

(a) that party shall provide measures in its marketing approval process to prevent those other person from:

a. marketing a product, where that product is claimed in a patent; or

b. marketing a product for an approved use, where that approved use is claimed in a patent,

During the term of that patent, unless by consent or acquiescence of the patent owner; and

(b) if the party permits a third person to request marketing approval to enter the market with:

a. a product during the term of a patent identified as claming the product; or,

b. a product for an approved use, during the term of a patent identified as claiming that approved use,

the party shall provide for the patent owner to be notified for such request and identify of any other persons.

As previously mentioned, not all embrace this new provision with enthusiasm. While some did find Australia's version of patent linkage is a lot less pro-brand name company as many have previously feared. For example, the commonwealth of Australia Senate Select Committee finds the "anti-evergreen" provisions i.e. imposing administrative penalty against pharmaceutical company engage in evergreening practice and special provision that allow attorney general to join any action to reclaim profit lost due to evergreen practice on behalf of Australian people. In committee's report, it states: " delay to marketing generic drugs as consequence of these change; however, slight, will have a cost to the PBS (Pharmaceutical Benefit Scheme), state government and consumers."

This requirement is implemented in AUSFTA implementation act of 2004 which includes an amendment of 1989's Therapeutic Goods Act. After the implementation of this provision, the marketing approval of a generic drug is "linked" with the patent status the brand name drug it is derived from. Particularly, a new section, 26B, 26C and 26D are added into Therapeutic Goods Act. 26B requires generic applicant for market approval with TGA to notify the original patent holder that its generic product is base on

and certify its product will not infringe a valid patent. In conjunction with the certification in 26B, 26C required original patent holder to certify that infringement action against generic company is conducted in good faith and have a reasonable chance of success. Furthermore, the proceeding will be conducted in a timely manner without unreasonable delay. Penalty of up to 10 million will be imposed if the certification is later found to be false or misleading and attorney general is allow to join action against false certification applicant to recover losses to the PBS (Pharmaceutical Benefit Scheme), Australia's medical care system. To further enhance government control over drug application process, section 26D stipulates that patent holder who seek interlocutory injunction against marketing of a generic drug will need government approval i.e. by serving a notice to attorney-general to do so. Attorney general may waive the right to be a party in the proceeding by giving a written notice to the court. As an deterrent against possible abuse of patent, 26(C)(8) specially stipulates that any damage suffered or costs incurred to the government as the result of granting an interlocutory relief that is later found by the court be an exploitation of patent , the mover i.e. usually the brand name company will need to bear any damage incurred as the result.

Obviously the new sections of 26C and 26D are Australia's line of defense against possible abuse of the new linkage system by the brand name company and ensure that their generic drug can still enter the market if government deems it as necessary or appropriate. Australia stand on the new linkage system as part of free-trade agreement is quite clear. As chief AUSFTA negotiator have stated before Australian Senate:

" We are not importing the Hatch-Waxman legislation into Australian law as a

result of the free trade agreement … (article 17.10.4) will not extend the time of marketing approval process, and it does not add or provide additional right to the patent holder in that process…"

Naturally, US's reaction to Australia's new amendments is less than warm. US trade representative made the following remark regarding Australia's implementation of AUSFTA:

"If Australia's law is not sufficient to prevent marketing of a product, or a product for an approved use, where the produce or use is covered by a patent, Australia will have acted inconsistently with the agreement … we also remain concern about recent amendments to selection 26B(1), 26C and 26D of the Therapeutic Goods Act of 1989. Under these amendments, pharmaceutical patents owners' risk incurring significant penalties when they seek to enforce their patent rights. These provisions impose a potentially significant, unjustifiable, and discriminatory burden on the owners of pharmaceutical patents. I urge Australian government to review this matter, particularly in light of Australia's international legal obligation. The United States reserves its right to challenge the inconsistency of these amendments with such obligation."

As obvious from tone of US trade representative, the pressure against Australian's stand on pro-generic drug legislation is enormous. However, Australia and Canada are not alone in this predicament. Korea as previous mentioned has also singed a free trade agreement with US and it too is imposed with an obligation to craft a patent linkage system. In Korean-United State Free Trade Agreement (KORUSFTA)'s Article 18. 9. 5, it stipulates:

"Where a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting safety or efficacy information, to rely on that information or on evidence of safety or efficacy information of a product that was previously approved, such as evidence of prior marketing approval in the territory of the Party or in another territory, that Party shall:

(a) provide that the patent owner shall be notified of the identity of any such other person that requests marketing approval to enter the market during the term of a patent notified to the approving authority as covering that product or its approved method of use; and

(b) implement measures in its marketing approval process to prevent such other persons from marketing a product without the consent or acquiescence of the patent owner during the term of a patent notified to the approving authority as covering that product or its approved method of use."

One feature that distinguishes US-Korean Free Trade Agreement is that it places original patent holder to notify the "approving authority" before the notification process takes place. This new feature allows for greater government oversight and control over patents that are listed in its pharmaceutical registry and can potentially prevent "sham" patents from being listed for the primary purpose to delay generic drug's entrance into market.

As shown from these three countries who had signed free trade agreement with US, patent linkage provision is an inevitable step. However, each country deals with this

new legal huddle in its own fashion.

Canada seems to tackle this problem in a more direct approach and designed regulatory measure specifically to curtail the potential evergreen practice by branded company. Canada's Office of Patented Medicines and Liaison is the main agency for monitoring and policing pharmaceutical patents and is the line of defense against abusive patent practice i.e. patent evergreening. While it is an effective agency but it is not above reproach especially from US based brand name drug manufacturer. The US Pharmaceutical Research and Development (PhRMA) claims that Office of Patented Medicines which under Health Canada, is inconsistent in its practice of listing and delisting patents from pharmaceutical patent registry. More particularly, PhRMA is complaining about Health Canada is slowly but consistently in limiting types of patents that can be listed in the registry. For example, patents are not eligible for being listed into Canadian patent registry if it doesn't meet some arbitrary timing requirement or not of certain types. Most of these eligibility requirements are not present in US Hatch-Waxman Act. Furthermore, from PhRMA believes Canada lags behind other G-7 nations in its effort in protecting intellectual property. For example Canada is the only nation in G-7 that does not provide any form of patent term restoration. In addition, PhrRMA also recognizes the disparity in their right of appeal between patentee and generic applicant. Under PM (NOC) regulation, patentee may take an action in summary proceeding against generic producer during its marketing approval process. However, if the court rules in generic's favor, no other alternative is available to patentee. The patentee can only start another proceeding, claiming infringement against generic company once its product has hit the market. In comparison, for a generic company, it may file for an appeal even if it initially does not prevail in a summary

proceeding.

Overall, PhRMA feels that Canadian government did not fulfill its legal obligation under NAFTA and TRIPs to provide “expeditious remedies to prevent infringements and remedies which constitute a deterrent to further infringements and “Canadian federal authorities should be encouraged by the United States Government to take immediate and effective measures to amend the current linkage regime to address the serious inequities and deficiencies...”

In the same PhRMA submission of 2009, Australia is also on the watch-list for the lack “effective” notification procedure and “discriminatory treatment for pharmaceutical enforcement action.” Specifically, FTA provision requires Australia to provide the original patent holder advance notice for any generic patent that is based on its patented product thus allow the patentee to seek injunctive relief before possible patent-infringing product enters the market. However, under current Australia’s regulatory regime, a.k.a. Pharmaceutical Benefits Scheme (PBS), for most of the situation, generic producer only need to notify Therapeutic Goods Administration. Furthermore, PhRMA is concern that potentially heavy penalty against only the patent holder in a infringement action is “unjustifiable, counterproductive, and violate Australia’s international obligations.”

7.3 Korean Comparison

Korean, on the other hand, is a good precedent for Taiwan. Korean like Taiwan is a single payer system much like Taiwan’s national health plan; therefore gaining access to its health insurance system is critical for any pharmaceutical company to have any

meaningful presence in the market. Similarly, pricing and reimbursement regime is closely set and monitor by government and any adjustment in this regime will drastically affect drug company's market share and profit margin.

Not surprisingly, several of PhRMA's major concerns are against Korean pharmaceutical pricing and reimbursement system i.e. Drug Expenditure Rationalization Plan (DERP). Some of its concerns include:

1) Under DERP, any generic product that enter Korean market will be imposed a 20% price reduction and this reduction is applied brand name product that is still under patent and is infringing by the generic. PhRMA urges the Korean government not to apply the 20% price cut for branded products that still have a valid patent.

2) Korean government re-evaluates all their currently listed drugs in a non-transparent manner and stakeholder is not given any information on how these evaluations are conducted.

3) Korean Free Trade Commission issued sanctions against PhRMA member companies who are engage in practice that are consistent with globally acceptable standard and practice. PhRMA believes these sanctions and investigation into PhRMA member maybe an unethical method via bribery to gain access to their "blockbuster" products' formulate or secure agreement to prescribe specific drugs. PhRMA is urging Korean government to implement its guidelines and rules in a non-discriminatory manner and consistent with international standards.

Industry and Politics

Brand name drug industry is a powerful entity and has strong tide with US government and is no stranger in using their powerful political tide into pressuring other

countries.

For example, in South Africa HIV is a rampant epidemic and medical supply is limited due to its high pricing. In 1997, South Africa government passed the "Medicines Act" that enables compulsory license on several effective branded HIV drug to be manufactured by local generic drug company. Brand name companies responded to this new legislation by seeking help from US trade representative to lobby for drug industry in, congressman Rodney Frelinghuysen filed a motion to ask congress not to let South Africa implement compulsory license on American drug and PhRMA lists South Africa into priority foreign country watch list. South African government is facing sanction from US government if it dose not comply with brand name drug industry's demand. The compulsory license requirement was subsequently defeated in South African parliament.

Under Clinton administration, brand name drug industry and South African government reaches a compromise, four out of five brand name company that have HIV drug is willing to sell their drugs to African people at only 20% of its original price and agree to special compulsory license to some of African generic drug manufacturer. In America, an average HIV patient spends about 15,000 USD annually on cocktail drug regime, so with 80% off from the American price, South African patient can receive the same drug regime in less than 3000 USD annually. However, average annually medical expense in Africa is about 10 USD per person.

Drug Company and Doctors

The relationship between drug company and doctors is a peculiar one[95]. Doctors need drug company to introduce and supply them the drugs they need. However, information from drug company is often twisted or presented as half-truth because not surprisingly drug company needs to make money. This creates a conflict between doctors and drug company, the company knows its sales tactic is effective but will never admit the information it supply to doctors can be misleading. Doctors, on the other hand, know what drug company is telling them is often just a sale pitch and misleading. However, close 80% of drug sales are from doctor's drug prescription and multinational drug company usual spend between 150 to 200 billion USD annually on personal selling to doctors.

7.4 Chapter Summary

Overall, patent linkage system is an unavoidable step when signing free trade agreement with US. Accordingly, each country formulates its own method to limit its possibility for abusive ever-greening measures by brand manufacturers. Canada has its NOC linkage regulation, while Australia imposed good faith requirement with a hefty penalty and venue for government intervention shall a patent abuse occurred. Similarly Korea controls the impact of patent linkage may bring with more intense governmental monitoring and control via its DERP that have a significantly bearing on which drug will be used by the hospitals.

Though these vigorous enforcements of anti-evergreen measure are justifiable from the respective government's perspective, these measurements may lead to US trade

[95] 柯雨利，促銷活動對醫師藥物選擇行為之影響，成功大學高階管理碩士在職專班碩士論文，頁10-12（2002）。

retaliation. Taiwan is on its way to sign a Trade and Investment Framework Agreement (TIFA) with US, which is ususlly the frist step of a free trade agreement, is bound to face a similar problem these countries have faced.

	United States	Canada	Australia	Taiwan
Patent Linkage Regulation	21 U.S.C. §355 (a) (b) (j)	PM (NOC)	Therapeutic Goods Act § 26B to 26D	None
Patent Disclosure Platform	Yes (Orange Book)	Yes	No	New Drug Monitoring List
Notice Period to Patentee	45 days	45 days	No	No
Application Stay Period	30 months	24 months	No	No
Market Exclusivity for 1st Generic Challenger	180 days	No	No	No
Specific Damage Compensation	No	Yes	Yes	No
Government Intervention	No	Yes (government agency as plaintiff)	Yes (as see fit by Attorney General)	No

Chapter 8: Pharmaceutical Landscape in Taiwan

8.1 Pharmaceutical Landscape in Taiwan

One of the most distinguishing features of Taiwan's pharmaceutical sector is the implementation of national health insurance which covers nearly 99%of Taiwan's populace. Its coverage includes clinic visit, hospitalization, out- patient service, chronic psychotic disorders, Chinese medicine, dentistry, operation, prescription drug, etc. Usually, a patient will need to borne between 5% ~10% of the medical expense. [96]

Due to its wide coverage, National Health Insurance's expenditure on prescription drug is subject to much scrutiny and debate since its inception. Under National Health Insurance, the pricing is determined by a team known as "Team of National Health Insurance Pharmaceutical Affairs." [97] This team is responsible to setting reimbursement pricing for each drug and regulation on how the reimbursement will be conducted and determine whether a said drug will be reimbursed at all or not. Team is comprised of officers from Health Department, clinical pharmacists, doctors and scholars. Each drug's reimbursement price will be determined from several factors includes: average price for a said drug in ten other countries, price of a similar drug that is already on the market or other literature references, etc.[98] Team holds a meeting once every month and average time for drug for reimbursement review is 6 months.

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[96] *See supra* note 32, at 104.
[97] 全民健康保險藥事小組。
[98] *See supra* note 74, at 105.

Drug that applies for reimbursement review is divided broadly into two categories: 1) new drug which is defined as drug that has "new active ingredient, new dosage, new administration route, or new therapeutic effect via drug combination." The other category is 2) drug that has the same active ingredient or dosage form that were already listed under drug reimbursement list. [99]

Furthermore, new drug under category one can be furthered divided into three types, they are:

1) Breakthrough drug.

2) Me-too drugs.

3) Line-extension drugs.

Reimbursement price for drug under each type are determined by taken into consideration of various factors. For breakthrough drugs, team will average prices of the said drug from ten countries [100] and set the median value as the maximum reimbursement price for the drug. For me-too-drug, the team will consider the amount of drug needed in a treatment cycle to determine its reimbursement price. Its reimbursement price shall never to higher than the intentional median gathered from breakthrough drug. Reimbursement pricing for Line-extension drug is determined by a specific formulate[101] published by Department of Health.

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99 藥價基準。

100 Ten countries are Britain, Japan, Germany, United States, Belgium, Australia, France, Sweden, Canada and Switzerland.

101 藥品規格量換算法，行政院衛生署衛生法規資料檢索系統：http://dohlaw.doh.gov.tw/Chi/FLAW/FLAWDOC01.asp?lsid=FL037963&lno=39（最後點閱時間：2013年6月20日）。

Moreover, since the expenditure on prescription drug places a heavy burden economically on the whole system, it is also Health Department's policy to push for wider application of generic drug. Ideally the pricing difference between generic drug and innovator drug is about 20% ~ 30%.[102] However, the reality is less than this simple.

Major Hospital System

In general, sales channel for pharmaceuticals can be divided into hospitals, clinics and pharmacy. Under hospital, it can be further categorized into research hospital, regional hospital and local hospital. By comparison research hospitals with their vast resources and reputation represent as the greatest consumers for drug. [103] Other than prevalent national health insurance, major hospital system i.e. the research hospitals is another distinguishing feature in Taiwan's medical care environment. To elaborate, major hospital accounts majority of medical service provided to Taiwan's public health, more specifically in 1998, major hospital served close to 28% of patient population and consume close to 50% of medical expenditure under National Health Insurance. [104] Just as in any market, when majority of market are occupied by only a few selected providers, it runs the risk of possible antitrust violations.

Major hospitals that basically dominate the whole medical care sector which taken up close to 40% of medical service market. [105] Due to their aggravated purchasing

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[102] *See supra* note 3, at 1.
[103] *Id*. at 62.
[104] 蔡穎吉，全民健保對西藥通路發展的影響， 靜宜大學企業管理研究所碩士論文，頁 8（2001）。
[105] 全民健保十五年，醫言堂網站：
http://blog.udn.com/tayiu/4113092（最後點閱時間：2010 年 6 月 9 日）。

power is able to negotiate bulk purchasing arrangements with drug makers, particularly brand manufacturers. Although reimbursement price is determined by the government sanctioned team of professional, there is still a wide margin between reimbursement price and its actual costs, especially for brand name drug. Due to its nature of being a new drug it is awarded with higher reimbursement price than generic, therefore more room for pricing manipulation. This phenomenon is the so-called "pricing black hole.[106]" To elaborate, due to the difference in bargaining power from different hospital systems, drug maker can offer different discount on the same drug for different hospital. It will result in the bigger the hospital the cheaper its bill for drugs will be. However, these hospitals charge its patient on its market price. Consequently, large hospital system is more likely to offer patient the more expensive drugs i.e. drugs that has higher margin and it's almost always brand name drugs which is why major hospital account more than 80% of brand manufacturer's annual sales volume. [107] By prescribing these drugs, hospital is also to make greater profits from them. As evident by the numbers, where generic manufacturers provide more than 70% of prescription drug used under National Health Insurance; however, its accounts less than 30% of its expenditure on prescription drugs. [108]

Pharmacist is subservient within hospital systems

Function of pharmacist within hospital system is not very prominent. In the hospital, doctor is usually the one who prescribes the medication and pharmacist simply prepares the medication as according to the doctor's instruction and rarely will

[106] *See supra* note 81, at 11.
[107] *See supra* note 83, at 7
[108] *Id*.

pharmacist in a hospital to suggest an alternative to a patient. Doctors basically monopolized on choices of drugs without check and balance from pharmacists.

Unlike in North America, family doctor system is not a very well implemented. People in Taiwan generally can choose freely which hospital or clinic they like to go to and the underlying mentality is: the bigger the hospital the better the service thus the bigger hospitals tend to attract a more significant patient flow as compare with clinics. [109] Unlike in the States where people usually go to their family physician when feeling ills and their physicians will direct patients to specialty doctors based on their professional opinion. Uniquely in Taiwan, patients themselves can decide which kind of doctors they like to see and can register accordingly based on their own judgments. Not surprisingly, many patients are not qualified to make such judgment and they end up seeing the wrong doctors and get send away to another. Many precious medical resources were wasted because of the lack use of family doctors and general health care quality suffered as the result overcrowding of patients.

In addition, the trend in Taiwan's medical care is such some of the larger hospitals occupies most expenditure in drugs whereas clinic and local hospitals are showing signs of decreasing.

According to survey done by Bureaus of General Health Care, the larger hospital occupies more than 80% of their approved drug expenses, whereas in countries such as United States and Japan the drug expenditure is more akin to 60:40 percentage.

Another obstacle about introducing generic drug is that since it takes at least 10

[109] *Id*. at 23.

years for patented drug to become generic and available to be marketed. By the time generic drug became available, pharmacist must obtain approval from both the doctor and patient to replace the more expensive brand drug with generic ones. As mentioned previously, doctor within major hospital system ultimately holds to power to decide which drug to be prescribed to the patients Therefore, it is difficult replace brand name drug with generic even if they are equivalent in terms of safety and effectiveness.

In light of this, many countries have devised a procedure that allows pharmacist with obtained consent from the patient to prescribe the equivalent generic drug automatically without approval of doctors.

8.2 American Regime:

Since using generic drug will save tremendous expenses in Medicare and Mediaid, consequently, American government is active in introducing generic drug that is parametrically equivalent of its Brand Name counterpart especially in lights of ever increasing expenditure in drug (it has increase about 10% from 1990 ~ 2006)

There are different systems employed by different states regarding this brand name drug replacement regime. It can be broadly categorized as either selective or mandatory.

In selective regime, unless otherwise specifically prescribed or asked by patient, pharmacist may choose a functional equivalent generic drug to replace the brand name drug.

In a mandatory regime, unless otherwise specifically requested by doctor and

patients, pharmacist must choose generic drug instead of brand name if possible.

In a 2008 survey by US Pharmacists, there are currently 40 states that choose the selective regime while 12 states use mandatory regime. As evident by this, the generic drug replacement regime will need government intervention to be truly effective.

8.3 Patent Linkage in Taiwan

Patent Linkage is an on-going issue and is a repeated agenda in the free trade talk (TIFA) with United States. Patent Linkage and legislation similar to Hatch-Waxman act has also being lobbied by International Research-Based Pharmaceutical Manufacturers Association (IRPMA).[110]

Nevertheless, there are already regulatory measures similar to HWA within the existing regulatory framework. Patent Act Article 53 stipulates that patentee may recoup two up to maximum of five years of patent term due to time lost in applying for market approval with government agency.[111] Regulation on data exclusivity is governed by Pharmaceutical Act Article 42-2[112] where new drug's information is protected for 5 years from being cited as reference for other drug's application. Paragraph 5 under the same article[113], generic drug maker also received experimental exception from conducting experiments and research on branded drug.

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110 李全芳，建構我國學名藥法制之研究，交通大學科技法律研究所碩士論文，頁 121（2010）。
111 專利法第 53 條第一項：「醫藥品、農藥品或其製造方法發明專利權之實施，依其他法律規定，應取得許可證者，其於專利案公告後取得時，專利權人得以第一次許可證申請 延長專利權期間，並以一次為限，且該許可證僅得據以申請延長專利權期間一次。」
112 藥事法第 40-2 條第 2 項：「新成分新藥許可證自核發之日起五年內，其他藥商非經許可證所有人同意，不得引據其申請資料申請查驗登記。」
113 藥事法第 40-2 條第 5 項：「…新藥專利權不及於藥商申請查驗登記前所進行之研究、教學或試驗。」

Currently, there is no patent linkage requirement. Department of Health is the authority in governing pharmaceutical's market approval. When a drug petitions for registration, its manufacturer will be required to produce a certification that warrant its drug application is free from infringing others intellectual properties, including trademark and patent. In addition, Department of Health will disclose patent registration number associated with the drug application upon its approval.[114]

Effects of Patent Linkage in Taiwan

Patent Linkage system is originally designed to protect patentee's interest while ensuring general public can have greater access to medicine. However, as we have seen from previous chapters, patent linkage has become a battleground between generic and brand name drug manufacturers where tremendous effort and ingenuity were spent in exploiting regulation loopholes and stalling litigation.[115]

Nevertheless, Taiwan's pharmaceutical industry is predominately generic manufacturers therefore policy favors too greatly to brand name company is indirectly detrimental to Taiwan's own pharmaceutical sector. Moreover while 180 days market exclusivity is a strong incentive to generic drug maker in US, it is hardly the case in Taiwan. Taiwan's market size is significantly smaller than US; therefore, generic drug maker can hardly recoup the same amount of revenue than if they were in the States. Taken into the consideration of costly legal battle the generic drug challenger will need to face, 180-day market exclusivity is much less appealing for Taiwan based drug

114 藥事法第 40-2 條第 1 項：「中央衛生主管機關於核發新藥許可證時，應公開申請人檢附之已揭露專利字號或案號。」

115 陳蔚奇，論美國專利連結制度於我國實行之妥適性，交通大學科技法律研究所碩士論文，頁 17-18（2010）。

company. Paragraph IV certification system works on generic drug maker challenges brand name drug company's patents, it is designed as a competitive measure to encourage further innovation in the industry by filtering out inappropriate patents.[116] However, in order to achieve such purpose, there must be a strong enough commercial incentive for generic drug maker to do so. Without strong incentive, the whole system will not function properly. Taiwan with its significant smaller market size, delay between drug received market approval and evolution by National Insurance Bureau and negotiation time for bulk purchasing agreement with major hospital systems, all these factors means additional time for generic drug from actually being "marketable," and greatly reduced 180-day market exclusivity's appeal to generic drug maker.

[116] *See supra* note 22, at 38.

Chapter 9: Pharmaceutical Litigation in Taiwan

9.1 Pharmaceutical Litigation in Taiwan

There are several types of litigation involving pharmaceutical products, mainly they are: trademark, copyright, patents and trade secrets.

In litigation involving trademark, its main issue will be focused on whether trademark of a generic manufacturer will confused customer and result in misrepresentation of its branded counterpart. Another battleground will be the copyrightability of packing insert. Lastly, as mentioned many times in previous chapters, patent right is also one of the most fought over ground between generic and brand name companies.

In association of patent right are trade secrets and competition law, these separate body of regulations can interact with each other on different level and form an intricate system of check and balances. The very nature of patent is a contractual one. It is a contract exists between individual and the State, in exchange of for disclosure of an individual's innovation, the States grants such individual a period of monopoly on the innovation. However, in the event such individual does not wish to disclose the innovation, innovation can also be protected as a form of trade secrets. On the other hand, patent right can also become an effective device in achieving unjust monopoly in some instance and this is where competition law comes in to re-balance the system.

In a pharmaceutical industry, clinical trial data and information on its supply chain

are two of most crucial pieces of information for a drug company. There are cases where true purpose of infringement litigation is to force the defendant to submit information about its supply chain to prove its innocence. The true motive of the plaintiff is to learn more about its main competitor's formulates by ascertaining its suppliers and cost-ratio, this information will help the plaintiff to adjust its marketing strategy accordingly. In practice, severing a warning letter to the opposing party is also one of the common tactics that preludes the full-blown legal battle in the pharmaceutical industry.

There are two crucial points in time for a typical pharmaceutical patent that may trigger a litigation. One is at when its patent expires and the other is at when its generic version enters the market. Most of the litigation between brand name and generic companies takes place at the time after branded drug's patent expires and before in-flow of generic drug enters the market. Two companies have conflicting interest at this point. From a generic drug company's point of view, naturally they will want to shorten this period so they may lunch their generic products as soon as possible, for example, many generic companies will conduct clinical trial near the end of patent's expiration or engage in a "design around" effort to avoid brand name drug's patent; while for a brand name company naturally, it will want to delay the entry for as long as possible. As previously mentioned, they will try to prolong its monopoly on doing a slightly modified version of its originally patented drug or try to apply for a new patent using a combination of patented drug with an old drug. These so-called "derivative drug" if patentable can give brand manufacturer de facto monopoly on the market.

In general, when a generic company petitions for market registration, brand name company can seek preliminary injunction to stall the review procedure on market

registration. Similarly, a generic company can petition for patent invalidation against brand name company at Intellectual Property Office (IPO) and argue for patent non-infringement in the Court. Even after a drug enters the market, a company can still issue warning letter or assert patent abuse against the other company. In summary, there are 3 stages in the typical legal battle among pharmaceutical companies:

1) Before the expiration of branded drug's patent, during this time, generic company will prepare necessary documents and conduct clinical trial by exerting experimental exemption in anticipation to market the generic drug as soon as the patent terms expires. Brand manufacturer will concentrate on making so many as possible derivative drug based on its patented drug.

2) In second stage, prelude to actual litigation, often the brand name company will petition for preliminary injunction. This measure is often the means itself, as the outcome of subsequent litigation is not important. If the court grants such petition, the drug in question will face a recall of products and effectively clear market of the competitors.

3) If a generic drug company is able to withstand all the challenges and successfully enter the market, there is one last trick up to brand company's sleeve. Brand company may still issue warning letters to users of generic drugs to hinder its sales effort.

In Taiwan, experimental exemption is codified in Patent Act Article 59 paragraph 1

and paragraph 2:[117]

The effect of an invention patent right shall not extend to any of the following matters:

1. Where the invention is put into practice for research, educational or experimental purposes only, with no profit-seeking acts involved therein...

The main issues here are whether the clinical trial conducted by generic company prior to patent expiration can be considered as a profit-seeking activities ;in other words, are these trials conducted for commercial purpose or not? The opponent asserts there is no actual income or profits gain from conducting these clinical trials by generic company while the proponent alleges the ultimate purpose for these trials is eventual commercialization of generic drug. This predicament is eventually solved with the arrival of Pharmaceutical Affair Act Article 40-2 paragraph 5 which states : "The patent right of the new drug shall not be applicable to researches, teachings, or testing prior to the application for registration by the pharmaceutical firms." The battleground shifts to another area, namely exactly is "research, teaching or testing" referring to by the Act. In the case of Eli Lilly（禮來）v. TTY Biopharm（東洋）[118] , in this case, defendant asserts adding water with active ingredient into solvable form is a process that involves complicated techniques and need to gather sufficient data from substantial amount of experiments in order to be successful. However, Court did not uphold this opinion, it

[117] 專利法第 59 條：「發明專利權之效力，不及於下列各款情事：一、非出於商業目的之未公開行為。二、以研究或實驗為目的實施發明之必要行為。」

[118] 台灣台北地方法院 93 年度智字第 77 號民事判決及台灣高等法院 94 年度智上字第 26 號民事判決（禮來對東洋）。

holds such technique is amounting to adding honey with water and will not sophisticated enough to be considered as ‘research and experiment.”

9.2 Taiwan’s Legal System

Just as in the States, patent evergreening is also a common tactic in Taiwan. Similarly by adjusting a patent’s method of delivery, intended use or even new combination, these measures can effectively prolong the effect of its “progenitor” patent. For example, in the case of Sanofi（安萬特）v. TTY Biopharm（東洋）[119] , the patent holder has the patent on Taxol and in 1981, patent holder further apply for ‘394 patent of Taxane. Since Taxol is not very soluble, it will need ethanol and other soluble agent to be better applicable in a clinical setting. Consequently, the patent holder applied for another patent, ‘742, making Taxol more easily applicable with a soluble agent. Generic companies, produced its own version of soluble form of Taxol and applied for patent, ‘471 in 2006 which is a mixture of Taxol with anti-gelling agent and soluble fluid. Unlike its branded counterpart, this generic version offers more solubility and is clinically more easy to use than patent holder’s ‘742 patent and its considered as more innovative than its predecessor. The generic company subsequently prevails in this lawsuit.

In the second stage of litigation battle, where patent holder is able to file claims for damages, or petition to stop or prevent further infringement. Damages are usually calculated based on the losses due the infringement. Stop infringement is usually done by taking the alleged infringed product off the market; in other incident, court may

[119] 台灣台北地方法院 97 年度智字第 38 號民事判決。

stop infringement by issuing injunction to stop production of alleged product all together. This stage can be further divided into two sub-stages, the first stage is filing for preliminary injunction against the infringed party and the second stage is the actual litigation itself. In order to warrant for preliminary injunction, the mover usually need to persuade the court there is a "severe and imminent threat" posed by the infringing party. Since such order is potentially disastrous to the other party is issued lightly, court will usually pose a substantial bond as the perquisite of granting injunction. For example, in the case of Takeda（武田）v. Genovate Biotechnology（健亞）, when the litigation erupts, the generic company ,which is Genovate in this case, has already passed the market review procedure and was on the eve of being awarded the market license. Brand name company moves quickly to petition for preliminary injunction against the generic, alleging patent infringement on patent drug's formula. Since court only has a very limited time to review petition for preliminary injunction, its judgment was hasty in this case and brand name's petition of preliminary junction was granted and issue notice to ministry of health to stop its review for generic's market license. The injunction was finally lifted after 4 years when the generic prevails in the lawsuit and was found non-infringing.

In another incident[120], where generic has already obtained market license but the brand name petitions for preliminary injunction, brand name also alleges infringement on its formula, patent on metabolite, and copyright infringement on its package inserts against the generic. However, after several appeals, the Court is persuaded by the generic company to lift the preliminary injunction by providing bonds. In exchange, generic is also to continue to sell its drug on the market.

[120] 台灣高等法院 97 年度抗更（一）字第 3 號民事裁定（武田對中化）。

The battle over preliminary injunction is often time merely the prelude to actual infringement proceeding. Two main issues in a typical infringement proceeding are: 1) the patentability of the patent in question 2) whether such patent is infringed by the defendant. In order for a patent to be eligible in other words patentable, such patent must satisfy three criteria, they are: novel, non-obvious and useful. In the case of pharmaceuticals, to qualified for usefulness is rather easy. Usually as long such pharmaceutical product is able to be produced with present technology, it will satisfy this criteria. As for non-obviousness, a commonly seen dispute arises when combining two known products together to form a new one. Whether such new product can satisfy the non-obvious requirement is often a subject of much debate. In practice; however, a commonly used examination criteria is whether such combination needs to conduct experiment in order to achieve it. If not, then it will not satisfy the novelty requirement.

Measurement use in a patentability dispute is to raise patent invalidation in Intellectual Property Office (IPO) or allege patent invalidity in the intellectual property court. In the case of Alendroid Acid used in the treatment of Osteoporosis, this patent of this drug is later found to be invalid. The patent invalidation actions were filed to both IPO and Intellectual Property Court. The main difference between filing in the Court and IPO was that if the patent was found invalid, such patent will no longer be effective; while, patent that found in invalid in the court, this decision is only binding to the opposing parties.

In the matter of infringement, infringement can be further categorized as “direct infringement” and “indirect infringement.” As in the case of Takeda v. CCPC[121] , brand

[121] 智慧財產法院 97 年度民專上字第 20 號民事判決（武田對中化）。

name alleged its patents on combination drugs and metabolite were infringed by the generic competitor i.e. CCPC. Regarding the combination drug infringement, brand name alleged generic can makes reference from its package insert to know about the drug combination this indirectly infringed upon brand name's patent. Branded company also alleged against doctors for prescribing a generic drug with another drug, such prescription of combining two drugs together, is an direct infringement against brand name's patent. On the issue of infringement of metabolite, brand name alleged when generic drug was metabolized by a patient, the metabolite resulted was patent-protected; therefore, such act constituted as a direct infringement against brand name and generic company constituted as contributory infringement by helping patient to engage in the infringing act. The court; however, did not accept such argument. The court held that brand name did not state a valid ground in direct infringement. Regarding indirect infringement, even though such reasoning was recognized by U.S. legislature; however, there are no corresponding regulations in Taiwan. Additionally, Taiwan's patent act also offers protection for drugs to prescribe combination of different drugs. Therefore, brand name's case of indirect infringement was also dismissed.

As mentioned previously, copyrightablity of package insert has surprisingly become another battleground for struggle between brand name and generic company.

In Taiwan, the term "generic drug", as stipulated in the "Guideline for Drug Review and Register[122] " Article 4 paragraph 2, generic drug is defined as pharmaceutical compound that has the same active ingredient, reagent, dosage and curative effect as the domestically approved Innovator drug. Such drug is a generic drug

[122] 藥品查驗登記審查準則。

of its branded counterpart. Taiwan's pharmaceutical industries, like most of other countries in the world, engage mostly in manufacturing and developing generic drugs. The development of generic drug industry is important for many reasons, one of the most important ones being: there are only a few countries in the world that is capable of independently researching a new drug. The discovery of an effective new drug is costly and lengthy business that few governments, let alone private enterprises, are able to afford. "The estimated average out-of-pocket cost per new drug is US$ 403 million." Consequently, by allowing the production of generic drug, local manufacturers can bypass the burden of high research costs and time, and provides general public with an effective drug which in turn may also foster the growth and development of domestic pharmaceutical industries. Furthermore, for country such as Taiwan where up to 98% of her citizens are covered under National Health Insurance, the incentive for lowering drug price is even greater. Since generic drug manufacturers incur less costs in making these drugs; therefore, it is easier for them to maintain profitability while continue to provide drugs reasonably affordable by the masses.

In recent years as will elaborate below, local manufacturers are increasingly facing more and more litigations from brand name manufacturers who allege copyright infringement on their package insert by generic competitors.

9.3 Package Insert, Label and Labeling

Package insert is the instruction slip that comes with a pharmaceutical product or medical device. According to Taiwan's Pharmaceutical Affair Act Article 25 , the term "label" refers to all the labels , package insert and packaging that come with the said drug or device. Comparatively, in "Federal Food, Drug and Cosmetic Act" (FDCA)

which has a slightly different definition on label and labeling. In this Act, the term “label” is used in a more constructive manner whereas the term “labeling” is much more encompassing. Label is defined as all labels, package inserts and any pictorial information printed on pharmaceutical containers while labeling can be done in the forms of instruction slip, pamphlet, video, voice recording, DVD, and etc. to convey necessary information regarding pharmaceutical products.

In Taiwan, the term “label” as it is stipulated in the Pharmaceutical Affair Act defined as label, package insert and packaging which is more akin to definition "labeling" used in the FDCA. Moreover, in the abbreviated new drug application (ANDA), the FDA requires labeling done by the generic manufacturer to be the "same as" its brand name counterpart. Article 20 Paragraph 1 to 3 of Guideline for Drug Review and Register, however, only requires package inserts to be of the same format or of an accurate translation of insert of the first applied manufacturer. It does not adopt the encompassing "same as" principle of the States on labeling in general.

According the Guideline, package insert usually refers to a paper slip that comes with a Pharmaceutical product. Its content should include:

1) Name of Manufacturer and address.

2) Product Name and Approval Number.

3) Batch Number.

4) Manufacture and Expiration Date.

5) Percentage of Active Ingredient and Application Direction.

6) Pharmaceutical Effects and Possible Side Effects.

7) Other important information at the discretion of Ministry of Health.

According to Article 20 of the Guideline for Drug Review and Register , which requires manufacturers who market the drug prior to 1983 (before the implementation of Drug Surveillance Program), to make its package insert to be of the direct translation as the one made by brand name manufacturer. As for generic drug that market after the implementation of surveillance program, the content of its package insert must be made in the same format as the insert made by first domestically approved manufacturer of the drug in question.

In the States, package insert is considered as part a drug's "labeling." According to HWA, drug labeling made by generic manufacturer must be the "same as" its innovator drug counterpart. Furthermore, in the case of Smithkline Beecham Consumer Healthcare, L.P. v. Watson Pharmaceuticals, Inc[123] , the defendant asserts the labeling section of Federal Food, Drug, and Cosmetic Act (FFDCA) requires generic labeling to be the same as the brand name drug as its argument for defense against copyright infringement . In Court's opinion, the same labeling requirement imposes by FFDCA is to prevent misrepresentation or error pertaining the information about the drug. The spirit of this act is to lower the costs for medicine and provide effective drugs to the general public by facilitating the marketing of generic drug. In Court's opinion, alleging label's copyrightability is essentially a competition measurement used by one drug company against another for greater market share. Therefore, in the conflict of interests between copyright law and FFDCA, the later should prevail. However, situation is a lot more complicated in Taiwan as it is in the States and Taiwan Courts went through many

[123] SmithKline Beecham Consumer Healthcare, L.P. v. Watson Pharmaceuticals, Inc., 211 F.3d 21 (2nd Cir. 2000).

debates to settle on the copyrightablity of package issue.

9.4 Package Insert's Copyrightability

According to World Intellectual Property Organization (WIPO), there are two primary purposes for the protection of copyright: To encourage a dynamic creative culture, while returning value to creators so that they can lead a dignified economic existence, and to provide widespread, affordable access to content for the public.

Nevertheless what entity or expression is copyrightable? According to Taiwan's Copyright Law Articles 3 and 5, it includes literary works on subjects in literature, Science, Art and other academic domain and in forms that includes but not limited to poem, sonnet, essay, novel, play, academic iteration, speech and other literary creations. Evidently from these definitions, as long as a creation objectively follows certain forms and on variety of academic subjects, it will fulfill the requirements to be copyrightable and warrants protection. Since copyright law is typically designed to protect a fixed expression or manifestation of an idea rather than the fundamental idea itself (which is often abstract and difficult to quantified).Under Copyright Act Article 10-1, it precludes abstract ideas, procedures, production process, discoveries, concepts and etc. to be copyrightable. To the question at hand, whether the package insert is copyrighted depends on two issues: Firstly, whether the content of package insert itself will fulfill originality requirement that warrants protection? i.e. insert's copyrightability is justified. Secondly if package insert is copyright protected, can the generic manufacturer assert fair use as a defense?

Originality

The originality of a literary work encompasses two essential elements: originality and creativity. Originality can be better understood as a requirement for independent creation. As long as the literary work in question is done independently not from copying an existing work, such work will have satisfied the originality requirement. Moreover, in considering the creativity criteria, the quality of the work is not a determining factor. The examination here adopts a minimal approach when considering originality: as long as the literary work had exhibited a minimal degree of creativity, such demonstration is enough to satisfy these creativity criteria and warrants the work in question to be copyrightable. The rationale behind such requirements is to protect works that is able to demonstrate author's uniqueness in expression or personality. Nevertheless, if the work in question has exhibited so little literary uniqueness then it is doubtful whether such work will be protected. According to Taiwan's Copyright Law Article 1, it states the purposes of copyright are to "protect the author's rights in equity with public good and to further countries' national development." Consequently, when considering whether a work warrants protection or not, one must also take concern of public policy into consideration. In other words, just because a literary work is rare or specialized doesn't necessary make it fulfills the originality requirement. This rationale is supported by a decision from Taiwan High Court[124]. In its judgment, the court states: " Although in a copyright case the originality standard is not as steep as the ones in patent law which emphasis on new design, new model and such, it nonetheless must fulfill certain intellectual function to be copyrightable. The work in question must be able to demonstrate author's uniqueness in expression and personality. For work that

[124] 台灣高等法院 91 年度 2342 號判決。

fails to meet such standard and has little intellectual function, it will be deemed not worthy for copyright protection." The Principle behind this judgment is straightforward. Over-generalization of copyright is detrimental to the cultural development of a society. Since over-generalization of copyright will hinder people's access to information and runs counter to the freedom of speech (as protected by Article 11 of the Constitution).

Presently, the package insert in Taiwan is made in pursuant to Article 75 of the Pharmaceutical Affair Act and Guideline for Drug Review Register which require generic drug manufacturer to make their package insert to contain a list of specific information and written in a very specific format, including its font size. Department of Health reserves the right to ask the manufacturers to add warning sign or notice on their packing when at its discretion, for the sake of public safety requires such action.

Evidently from these regulations, the writing style and information on package insert is strictly monitored and regulated by law. Additionally, since generic drug's main chemical component is also identical the innovator drug that it is based on. It is only natural their inserts will be highly identical as well. When an idea and its expression are inspirable and indistinguishable or when an idea’s means of expression are limited in only number of ways, this idea is effectively “merged” with expression as defined in "the merger doctrine of idea and expression.” Under such circumstance even if other works are highly identical to the one in question, those works will not constitute as copyright infringement. Package insert, by its very nature and manner of writing, will be unable to demonstrate its author uniqueness in expression and personality which is the essential element to be copyrightable.

In the past there were several judicial decisions regarding the copyrightablity of

instructional manual which package insert in its nature is manual-like.

In a Supreme Court judgment[125], the Supreme Court held that "An instruction manual for a mechanical arm which contains an introduction on method of operation, lacks originality and is not protected by copyright." However, not all courts were uniform in this approach, on the contrary, a Taiwan High Court decision[126] held that the package insert is qualified as literary work under the existing copyright law.

Court defines package insert as a description made pursuant to Article 26 of the Pharmaceutical Affair Act and can be commonly refer to as drug instruction manual. Package insert is made from data collected in officially recognized pharmaceutical text and research papers which contains information regarding the said drug or compound's pharmaceutical effects, formulation, prohibitions and etc. Its written style and content are strictly regulated and scrutinized by Department of Health in accordance with Guideline for Drug Review and Register. The manner of its expression satisfied the requirement of literary work (as stipulated in Copyright Act Article 3 and Article 5 Paragraph 1). Additionally, package inserts contains information regarding drug's curative effect, dosage instruction, sides effects, overdose information, cautionary notices and etc. These information can only be gained through series complex scientific experiments in the area of pharmacokinetic and related disciplines. The researcher will need to filter through complicated and series of data to arrive at the desired information. In other words, the information on package insert can be understood as the fruits of many hours of tirelessly research from mountains of data.[127] Furthermore, getting these

[125] 最高法院 89 年度台上字第 7233 刑事判決。
[126] 台灣高等法院 94 年度智上字第 17 號民事判決。
[127] 內政部 81 年 11 月 17 日（81）台內著字第 8119189 號函。

data, despite its hard work is only half way to produce package insert. These scientific jargons will later need to be translated by highly trained professionals into plain language so the average consumers can understand. The process of translation is an expression of certain degree of originality because wording on package inserts is written by trained personnel based on their professional judgment. In other words, package insert is not merely an instruction or abstract idea about the drug. Therefore, package insert should be categorized as an academic iteration and thus be copyrightable

On the contrary, in another High Court decision[128], it reasons: Although package insert is required to submit for review by Department of Health and the agency may modify or delete insert's content at its own discretion, Court held such procedure is in place to protect public interests. The degree of such modification usually will not severely alter the spirit of the original author; consequently, alteration if any will not affect insert's copyrigtability. Since this procedure is administrative in nature which will make package insert as a form of "official document" as defined in Article 9 of Copyright Law and make it not eligible to be copyrightable.

9.5 On Judicial Fronts

As evident by previous discussion, Court's holding on package insert is highly diverse. In Taiwan violation of copyright will incur both civil and criminal liability (as stipulated in Copyright Act Article 84, 88, 91 and 92.) Currently there are four kinds of judicial holding regarding package insert's copyrightability:

[128] 台灣高等法院台中分院 95 年度智上字第 9 號民事判決。

1) No criminal liability.

2) Package insert is copyrigtable and is civilly liable.

3) Package insert is copyrigtable but constitute no civil liability.

4) Package insert is not copyrightable or did not constitute as a Copyright Violation.

No Criminal Liability

Compare with various holding in civil cases, prosecution's point of view in this matter is more or less uniform regarding criminal liability of infringing package insert. In most cases, the prosecution holds package insert is not copyrightable. On the civil front, currently there is the only one judgment[129] that holds package insert is copyrightable and the generic manufacturer is civilly liable to the brand name company for damages. In High Court's opinion: "Guideline for Drug Review and Register is an administrative regulation, hierarchically its power cannot super-precede that of Copyright Law." Therefore, generic manufacturer's translation of innovator drug's package insert violates copyright. This holding; however, was later not followed by another judgment[130] which dismiss the appellee's action (the plaintiff in pervious action). This decision, nevertheless, did not solve the lingering doubt about package insert's copyrightability and may send a misleading message to drug manufacturer that legislator wishes to exempt Guideline for Drug Review and Register form application of Copyright Laws. Guideline for Drug Review and Register is a type of legal order which according to most jurisprudence scholars has the same governing power as other laws

[129] 台灣高等法院 93 年度智上字第 81 號判決。
[130] 同註 126。

but of a lower legal status. By definition, a legal order "shall not transgress the scope of such authority or divert from the legislative purposes of its enabling law." Nevertheless, in a certain condition where such legal order was specifically authorized and within the scope of its authority or legislative purpose, it is possible a legal order may of the same legal status as a full-fledged law such as the Copyright Law.

There are currently two other notable judgments[131] that supports package insert's copyrightability. These two judgments were among the very first to recognized package insert as copyrightable. In these judgments, the Courts held: “In a drug's package insert it contains information regarding cautionary notice, side effects, dosage and terms for treatment, and length of drug's effect. These data were more than mere numbers. It represents the fruit countless hours of scientific experiment and research. Consequently, the language used on the insert is an objective form of scientific expression (chemistry) which is readily copyrightable under Copyright Law." This position is supported by numerous judgments and decisions.[132]

Even for Courts that hold package insert to be copyrightable but majority of Courts held it to be not civilly liable, the reasons can be summarized as the follow: 1) Good Faith Reliance of Law 2) An act pursuant to legal order and 3) No illegality.

In a district Court decision[133] , the Court holds the inserts made by brand name manufacturer and the translated versions made by generic manufacturer both are copyrightable. However, the generic manufacturer did not commit infringement because

[131] 台灣高等法院94年度智上字第17號判決，以及台灣南投地方法院94年度智字第3號民事判決。
[132] 台灣高等法院台南高分院 94 年度上聲議字第 810 號刑事處分書，以及台灣台北地方法院檢察署 2006 年 12 月 18 日 95 年度偵字第 25746 號不起訴處分書。
[133] 同註 126。

“the generic manufacturer made their insert in reliance of law based on good faith and making or translating of package insert is required by Pharmaceutical Affair Act and Guideline of Drug Review and Register, which impose an obligation on the manufacturer to follow; at the same time, it also inadvertently impose an obligation onto the brand name company to endure."

In another judgment from High Court[134] , the Court holds that the insert is “made in a good faith reliance to the current legal and is not illegally infringing upon copyright" and "action undertook in order to fulfill a legal order shall not be construed as illegal.” Furthermore, the Court raises another issue, “since the generic manufacturer's insert is based mainly on the research done in abroad, the marking of this insert has no bearing on the original maker's potential market and present values. It is qualified as a type of “other necessary legitimate” use as stipulated in Article 52 of Copyright Law which constitutes as a type of reasonable use to use as a defense against copyright infringement."

Another holding is that package insert is a type of official document thus its content is not copyrightable. This position is upheld in both High Court[135] and prosecutors’ office [136]. Both hold the package insert is a type of official document, and according to Article 9 paragraph 1 of Copyright Law, official document is not copyrightable. Additionally in two other decisions, [137] the Courts hold: "Although Department of Health has the right to delete or modify insert's content, such

[134] 台灣高等法院 94 年度智上字第 17 號民事判決。
[135] 同註 128。
[136] 台南地方法院檢察署 94 年偵字 7716 號不起訴書。
[137] 同註 131。

modification is not enough to alter the original spirit of expression intended by the author; therefore, it has no bearing in insert's copyrightability ."

"Official document" is defined as documents used in the bureaucratic function, it is defined in Act Governing the Forms of Official Documents Articles 1 and 2. In Article 2, it specifically includes documents use between civil entities and agency. Its formats include document template, notice, certification and etc. As evident from such Act, package insert bears many elements that can be qualified as a type of official document. Furthermore, since Department of Health's policy is to standardized package insert by posing bulletin to drug manufacturers regarding formats and content of an insert should have. This action is one step further in pushing package insert's nature to be more akin to official document.

Reasonable Use Defense

In a High Court decision[138] , the Court bypasses the issue regarding insert's copyrightability and holds in favor of the generic manufacturer, the Court's rationale is as such: "any action undertaken to fulfill an obligation imposes by Law i.e. the making of package insert based on a good faith reliance of law, cannot be construed as a copyright infringement." and "action taken pursuant to a legal regulation is within the scope of reasonable use, therefore there is no infringement." Nevertheless, this decision was later abolished by Supreme Court. In a Supreme Court decision[139] , it puts forth a new test for ascertaining whether reasonable use will prevail against copyright infringement. Supreme Court requires lower Courts to ascertain the legal

[138] 高等法院 96 年度抗字第 1619 號民事裁定。
[139] 台灣最高法院 96 年度台抗字第 939 號民事裁定。

relationship between the parties by investigating the criteria for preliminary injunction i.e. will the movant (party who filed for the injunction) suffer substantial threat of irreparable harm or injury if the injunction is not granted ? In considering substantial threat of irreparable harm, the Court must also taken into the account of likelihood of success based on the merits of the case, public interest and the "balance of harm" test i.e. weighting the threatened injury to the party seeking the preliminary injunction as compared to the harm that the other party may suffer from the injunction. If the case is without merits or the support of material fact then there is no need for considering other factors and motion for preliminary injunction will be denied. In the case of Smithkline Beecham Consumer Healthcare, L.P. v. Watson Pharmaceuticals, [140] Inc. Brand Name Company seeks preliminary injunction against a generic manufacturer by alleging that the generic drug comes with a user guide and recording and both are almost identical to the ones made by brand name company. The Court held this case is entirely void of merit and deny brand name's motion for injunction. In other words, Court held in this case, there is obviously no infringement or the right sought is non-existent therefore no chance of winning as injunction can be denied simply because the moving party has no chance of winning the case.

Although in this case, an American Court held the user guide and recording made by brand name company is not copyrightable, whether this reasoning is also applicable to Taiwan is doubtful. Since labeling definition under Federal Food, Drug and Cosmetic Act is much broader than Taiwan's Drug Act. The Labeling in U.S. includes pictures, prints and tables that comes within and on of the drug packing. This definition is further

[140] SmithKline Beecham Consumer Healthcare, L.P. v. Watson Pharmaceuticals, Inc., 211 F.3d 21 (2nd Cir. 2000).

broaden by the FDA to include user guide, instruction manual, recording and other literary or non-literary articles that use to explain the drug's property. Furthermore, Abbreviated New Drug Application (ANDA) established in the Hatch-Waxman Amendment imposed a "same labeling requirement" for the product description between brand name and generic maker in order to speed up the introduction of generic drug to the public. Since the U.S. system and definition of label is clearly very different from ones in Taiwan, it will be over-generalizing to assume package insert is copyrightable under American law is somehow transferable to our system of laws.

"Not an intentional infringement and package insert possesses no originality" is another stand in this dispute. As discussed previously, prosecution is somewhat more unified in the issue of insert's copyrightability. Cases are dismissed as not eligible to be copyrightable for two reasons: 1) Content and format of package insert is made in accordance with the requirement of the laws 2) the managing authority i.e. Department of Health has the ultimate authority to review and amend the insert's content and format. In essence, package insert dose not demonstrate enough originality to warrant the copyright protection.

Additionally, in two other prosecution's investigation report[141] , both prosecution offices held: information on package insert is required to strictly follow criteria set out in Guideline for Drug Review and Register and the generic manufacturer has neither the will nor the intention for committing copyright infringement.

[141] 台灣台南地方法院檢察署 94 年偵字第 7716 號不起訴書，以及台灣台北地方法院檢察署 95 年偵字第 25745 號不起訴書。

A decision[142] from Taiwan High Court Taichung Branch is currently the only judgment that held package insert as not copyrightable. Its rationale is as follow: "generic manufacturer makes its package insert in a good faith reliance of law, therefore it cannot be construed such act as infringement,""the package insert has the essential characteristic of an official document; therefore, it is not copyrightable." In addition, since the format and content of package insert must be written in the manner as required by the regulation, it lacks the personality and uniqueness of the author which is an essential element for a work to be copyrightable; furthermore, package insert comes with the drug and has little intellectual function. Due to its very nature, package insert is severely limited in ways of its expressions. For the forgoing reasons, package inset can't satisfy the originality requirement to be eligible for copyright protection. Additionally, package insert can be considered as an accessory of the drug it accompanies. According to Article 68 of Civil Code: "The disposition of a principal thing extends to its accessories," In other words, if the principle thing i.e. the innovator drug had already expired its period patent protection; consequently, if the principle is no longer protected by any legal right nor shall its accessory (package insert) to be protected.

9.6 Chapter Summary

In summary, author believes the package is not copyrightable. Even if it is copyrightable, the generic manufacturer can argue reasonable use as a valid defense. The reasons as following:

[142] 同註 126。

1) In Supreme Court decisions[143], Courts stated: "Instruction manuals that simply contain the direction, description or explanation regarding the product or manuals for product of the same category due to their very nature must use in similar ways which will result in a limited ways of expression. Consequently, such work will not have satisfied the originality requirement to be copyrightable. “Similarly, package insert that contain a simple description regarding the direction, purpose, characteristic of the drug, it will inevitably to other inserts for other drug in the same category and its methods of description and manner of expression will be limited in only so many ways and such work is therefore not copyrightable.

2) Package Insert is considered as the accessory to the drug. In itself, package insert has little value and has little intellectual function. Its main purpose is to serve public inserts by conveying necessary information such as ingredients, curative effect, and side effects regarding the drug to the consumers.

3) The purpose of package insert is to protect consumer's safety. Pharmaceutical Affairs Act Article 39 paragraph 1 and 4 requires: “The manufactured or imported drug should submit its original insert and Chinese translation to the managing authority for review and register. In addition, Article 20 of Guideline for Drug Review and Register also has place specific requirement regarding insert's specific format. In other words, the law and regulation have imposed various requirements and standards regarding the making of package insert. These regulations require package insert to be written in a standardized formats and contain very specific information. These requirements have made package insert more akin to official document than literary works; thus, not copyrightable entity under Article 9 of Copyright Act which precludes official document

[143] 最高法院 93 年度台上字第 5206 號刑事判決，以及同法院 95 年度台上字第 684 號民事判決。

to be eligible for copyright.

4) Since the writing style and wording of the insert is dictated by law, it lacks unique expression and personality of the author that a literary work commonly requires to possess such elements therefore for lacking these element, such work will had met the originality standard; thus, not copyrightable. Additionally, considering the wordings on inserts aside from specialized terms, there is not enough room left for the insert to be qualified as serving any intellectual function.

5) Derivative works i.e. translation of package insert which is commonly required for imported drugs. For the original work, it only needs to demonstrate minimal amount of creativity and originality to be copyrightable; however, for the derivative works such as translation work, a much steep standard is imposed. For the translated work to be protected by copyright the translator needs not only persevere original author's creative originality, such work must also demonstrates the translator's own uniqueness in expression. Since package insert is clearly not able to demonstrate its translator's uniqueness in expression (inserts are required by law to be identical to the original); therefore, insert is not copyrightable.

Reasonable Use

Pursuant to Copyright Act Article 52: "Within a reasonable scope, works that have been publicly released may be quoted where necessary for reports, comment, teaching, research, or other legitimate purposes." and Article 65 of the same Act: "Fair use of a work shall not constitute as an infringement on economic rights in the work. In determining whether the exploitation of a work complies with the provisions of Articles 44 through 63, or other conditions of fair use, all circumstances shall be taken into

account, and in particular the following facts shall be noted as the basis for determination:

1. The purposes and nature of the exploitation, including whether such exploitation is of a commercial nature or is for nonprofit educational purposes.

2. The nature of the work.

3. The amount and substantiality of the portion exploited in relation to the work as a whole.

4. Effect of the exploitation on the work's current and potential market value."

The following is the analysis of whether use of package insert can be considered as a fair use defense by fulfilling requirements set in Article 65 of Copyright Act.

Nature and Purpose of Package Insert

Package insert is made for the sake of public health and consumer safety. The requirements on its content and format set in Pharmaceutical Affairs Act is for the purpose of familiarizing consumers regarding drug's pharmaceutical effects, ingredients and direction for use. Package insert is noncommercial in its nature and not able to be sold independently from the drug it comes with. In other words, package insert serves public good and is not profitable; thus, is eligible for reasonable use.

Amount and substantiality of the portion exploited in relation to the work as a whole is another determination factor when considering fair use defense. For the issue at hand, package insert made by generic manufacturer is based on the one made by manufacturer of innovator drug. According to Justice Leval, generic maker’s use of

package insert can be construed as fair use, his rationale is as follow:

1) Generic manufacturer has legitimate reason for making package insert:

As already previously discussed, law imposes a compulsory obligation to the generic manufacturer to make their inserts to be highly similar if not identical with insert that comes with innovator drug. It is not beyond belief, if without such restriction, generic manufacturer may even be able to make better written insert than the original.

Secondly, if allow brand name company is able to sue for copyright infringement after patent term on its innovator drug has expired, it essentially allows brand manufacturer to illegally extend its patent term which is in contrary to the purpose of public policy i.e. improving public health by make proven and effective a drug available public at much lower price than innovator drugs.

Thirdly, staple article of commerce in this matter is the drug itself, is not package insert. Therefore, court by allowing fair use on inserts will not discourage brand manufacturers willingness to create new drugs.

Lastly, since package insert itself has not particular value and is not a commercially independent article. By allowing its fair use will not be detrimental to brand name company's potential market.

Other Legitimate Purposes[144]

[144] 著作權法第 52 條。

According to Pharmaceutical Affairs Act Article 39 is the authority that Department of Health uses to establish Article 20 of Guideline for Drug Review and Register. In this guideline, it stipulates, in order for a generic manufacturer to obtain an approval certification, its package insert must be a direct translation of the foreign insert if innovator is imported or is of the same format of the first domestically approved insert. Furthermore, the generic manufacturer must also submit report regarding its generic drug's bioequivalence comparing with innovator drug it is based on. As required by Drug Act Article 42.

In other words, generic manufacturer is required by laws i.e. Drug Act and Guideline for Drug Review and Register, to make its package insert a genuine translation or copy of insert made by brand manufacturer or the first generic manufacturer who has obtained domestic approval certification. The said manufacturers will also be required to submit a bioequivalence report along with brand manufacturer's package insert to Department of Health for review and approval. From legal theory of good faith reliance's perspective, it is unfathomable to hold generic manufacturer liable to copyright infringement since the generic manufacturer is required by law to make a direct translation of brand manufacturer's insert

Moreover, the content on the insert such as application direction, dosage, possible side effects, cautionary notices and etc, this information are only relevant to its accompanied drug. The insert itself can't be sold independently and has little if any potential market value. According Copyright Act Article 65 Paragraph 2," Effect of the exploitation on the work's current and potential market value" is insubstantial. Subsequently, the use of insert can be qualified as other legitimate use under fair use

doctrine. (Copyright Act Article 52)

In summary, author believes: Even if package insert is copyrightable under the most lenient interpretation as a form of scientific expression, the generic manufacturer can, nevertheless, asserts fair use as a defense.

9.7 Other Litigation Claims

In a case of Sanofi-Aventis v. TTY Biopharm, brand manufacturer which is Sanofi-Aventis in this case sues TTY Biopharm, a generic manufacturer for infringement. Generic submits its data to support its non-infringement claim and also requests a protective order from the Court not to allow the opposition i.e. Sanofi-Aventis to review its data and files associated with alleged infringing drug. Brand name company appeals this decision many times but all were denied by the Court. The Court holds that these data and files are the trade secrets of the generic company because these data includes information on research, production method, suppliers and government registration. There data were instrumental to generic company's business operation and warrants trade secret protection. Court is therefore duty-bound to prevent sensitive information on generic's supply chain and pricing strategy from disclosing to other competitors.

The following is a table of recent litigation between local drug manufacturer and international drug company:

Local Manufacturer	**International Manufacturer**	**Litigated Product**	**For Treatment of**	**Litigation Result**
科化生技	Merck	Alendronate Sodium Trihydrate	Osteoporosis	Local Victory
Genovate	Takeda	Vippar	Diabetes	Takeda pays 50 million in damages
TTY Biopharm	Lilly	Gemcitabine	Breast & Prostate Cancer	Settled
TTY Biopharm	Sanofi-aventis	Taxol injection	Cancer	TTY Victory

*Source: http://www.jcpatent.com.tw/news_detail.asp?seq=372

After Market

Even after drugs enter the market, the battle between the brand name and generic continues unabated. Two preliminary methods include: 1) preliminary injunction misuse claim and 2) use of warning letter.

In the case of Genovate Biotechnology v. Takeda Pharmaceuticals[145] , market registration for generic company is approved by the authority but was stalled again because brand name when it moves for a preliminary injunction against generic manufacturer. The contested drug is Vippar which an oral medication used in treatment of diabetes. Genovate successfully makes a generic version of Vippar of which Takeda Pharmaceuticals is original patent holder. Generic Vippar application was reviewed by

[145] 最高法院 98 年度台上字第 367 號民事判決，以及台灣高等法院台中分院 96 年度智上字第 18 號民事判決。

Department of Health and was on the verge of obtaining market certification when Genovate was sued by Tekeda for infringing its patents on drug combination. The entrance of generic drug was stalled for four and half years before Court finally found no-infringement in favor of Genovate. Afterward, generic filed for damage claim against brand name and was award for half of billion dollars in damages. In this case, Takeda Pharmaceuticals argues against this decision and alleges it is within its legal right to petition for preliminary injunction based on a valid right. Therefore, its move for preliminary injunction should not constitute as an abuse of its right. The Court held; however, "the use of improper methods that cause the disruption of commercial order shall constitute as an abuse of right and is an act against good faith and such act shall be governed by fair trade act." Court's rationale is as follow: Even though the granting of preliminary injunction within the power of the Court. However, if the mover knows there is a defect in its right and intentionally or should have known not to apply for such injunction but did it anyway. Such mover should be held liability for damages resulted from an improperly issued injunction.

Warning Letter

Warning letter is a competition device and has seen many uses especially in highly competitive products such as pharmaceuticals. It is usually served by one company to its competitor's potential clients or purchaser. In pharmaceutical sector, warning letter is usually served to major hospitals. [146] The fundamental purpose of a warning letter is to prevent third person from purchasing infringing goods and function as an effective

[146] 蘇嘉瑞等著，「藥品智慧財產權紛爭之實務研析」，發表於「藥品專利訴訟實務分享及藥廠業務行銷法律風險」研討會，頁 6-7（2011）。

deterrent to ward off potential buyers. If serving such warning letter without restraint, it can cause severe disruption in commercial order. Consequently, Executive Yuan of Taiwan has announced a guideline which governs the manner and conditions when severing these letters. The subject matter of this guideline includes everything from warning letter, lawyer letter, and public notice to anything that can potentially affect the commercial order. According to this guideline, any party who wish to serve warning letter to other party must first obtain at least a prevailing judgment in district court or have conducted professional assessment report on the alleged infringing product to establish ground before serving warning letters. In addition, before serving these letters to third party, the plaintiff must first serves a notice to the accused. Failure to comply with this requirement can constitute a possible violation against Fair Trade Act Article 9, 21, 22 and 24.

9.8 Summary

Taiwan's pharmaceutical sector is still very young compare with the States and it still trends strongly toward generic drug manufacturing. Thus, it is very vulnerable to interference and disruption caused by brand manufacturers. Moreover, Taiwan's unique hospital systems and prevailing national health insurance system provide further competitive edge for innovator drug manufacturers. Due to these circumstances, government intervention will be especially important to balance the legitimate interests for innovator drug while protecting the needs for generic drugs.

Chapter 10: Conclusion

10.1 Brave New Market

From 2011 and onward, many prominent innovators drugs are facing its patent term being expired. The following is a table summary:

Name of the Drug	Term Expiration Year	Treatment	Manufactured by	Estimated Commercial Value
Lipitor	2011	Cholesterol	Pfizer	5329,000,000
Zyperxa	2011	Antipsychotic	Eli Lily	2,496,000,000
Levaquin	2011	Antibiotic	Johnson & Johnson	1,312,000,000
Concerta	2011	ADHA/ADD	Johnson & Johnson	929,000,000
Protonix	2011	Antiacid	Pfizer	690,000,000
Plavix	2012	Anti-platelet	BMS/Sanofi-Aventis	6,154,000,000
Singulair	2012	Asthma	Merck	3,224,000,000
Seroquei	2012	Antipsychotic	AstraZeneca	3,747,000,000

*Source: Wingu Research Intelligence @blog.wingu.com

In the coming years, the role of generic manufacturer will become increasingly demanding as more and more prominent innovator became available to generic development.

10.2 Future Prospect and Conclusion

As of writing of this paper, the struggle between brand name and generic manufacturers remain unabated and will likely to be for the coming years.

Several issues raised in this paper remain contested. They are:

1) Legality of reverse payment.

2) Legality of Brand name manufacturer voluntarily delisting its registration from Orange Book.

3) Use of authorized generic.

4) Will a final court decision and declaratory judgment necessary?

Legality of Reverse Payment

In a recent Supreme Court ruling in *FTC v. Actavis*,[147] the Court put forth there are several factors to consider when determining whether reverse payment violates antitrust rule or not. These factors includes: 1) size of patent holder's payment 2) its scale in relation to payor anticipated future litigation costs 3) its independence from other services for which it represents payment and 4) the lack of any other convincing justification. As mentioned in previous chapters, before this judgment in governing authority in the pay-for-delay or reverse payment is the case of *In re Cardizem CD*[148], which holds any type of reverse payment, is per se illegal. This issue is followed by

[147] FTC v. ACTAVIS, INC. ( ) 677 F. 3d 1298, reversed and remanded.
[148] *In re* Cardizem CD Antitrust Litigation, 332 F.3d 896 (6th Cir. 2003).

another case, *In re K-Dur*[149], Federal Court proposes a rule of reason balancing test. Any resettlement involving brand company paying generic manufacturer not to market its drug for a period of time will be considered as have violated antitrust regulation unless brand name company can prove there is a genuine pro-competitive benefits resulted from such payment.

In Supreme Court's holding of *FTC v. Actavis*, the Court reject all the aforementioned tests put forth in other Courts. Supreme Court found these tests too are either too simple or still insufficient to justified immunity from antitrust law. More specifically, lower Courts' scope of patent is not sufficient to fully grasp the anti-competitive effect resulted from these complex settlement; while, rule of reason balancing test is too broad to be employed consistently. The majority (5 votes for FTC and 3 against) in Supreme Court holds: "that reverse payment settlements are not presumptively unlawful and although patent-based settlement agreements can sometimes violate anti-trust laws, the Court declined to apply an all-or-nothing rule regarding these agreements. Instead, the Court stated that there are five considerations that should have allowed the consideration of FTC's case. These considerations are: 1) that specific restraints in the settlement agreement had the potential to adversely affect competition; 2) that certain anti-trust consequences will sometimes prove unjustified; 3) that if a reverse payment settlement can cause anticompetitive harm, the patent-holder likely has the power to bring about that harm as well; 4) an anti-trust claim may be more administratively feasible than the lower court believed; and 5) the fact that a large, unjustified reverse payment settlement risks anti-trust liability does not prevent litigating parties from settling their lawsuits. The Court held that these considerations outweighed

[149] *In re* K-Dur Antitrust Litigation, 689 F.3d 197 (3rd Cir. 2012).

the lower court's decision to provide anti-trust immunity to reverse payment settlements. [150]

Use of Authorized Genetic

As writing of this thesis, this issue remains undecided. Between year of 2004 ~ 2008, there are total of 38 settlement involving Authorized Generics. In 20 cases, Brand manufacturers decide not to compete with generic manufacturer via authorized generic drugs. Instead, brand name grant exclusive license to generic manufacturer. Generic companies in return agree not to make their own drugs but are supplied exclusively by brand manufacturers.

This is actually a win-win situation for both companies. Business-wise brand manufacturer uses a very different business mode as compare with its generic competitors. As a manufacturer of innovator drugs, brand manufacturer is adopt at research and development; while, generic manufacturer are more trend toward channel marketing and pricing strategy. Therefore, brand manufacturer is less familiar with the business environment of selling generic drugs and its margin may even be too low for brand name company to be justified for such venture economically. Therefore, leaving the act selling of generic drug to generic manufacturer while brand manufacturer still ripe the benefits of being an exclusive supplier is a more economically favorable choice for both companies.

In conclusion, in the coming years, the battle between generic and brand name companies will only get more intense as many prominent innovator drug became

[150] FTC v. Actavis Inc., *available at* http://www.oyez.org/cases/2010-2019/2012/2012_12_416.

available for grab. The abovementioned issues will undoubtedly become some of the most contested grounds in this war. From Taiwan's perspective, even though patent linkage system is still in its infancy. If signing an FTA with the States is an inevitable step then whatever litigation battles and arguments take place in the States, will one day make their appearance on Taiwan's legal scene[151] as well. The author believes it will serve Taiwan's Court well by observing how these arguments unfold in the States and make the judgments in accordance with unique local elements in order to maximize public good. The essential nature between brand name and generic drug company is, after all, a tug-of –war between two spectrums of public goods: the needs for innovation in medicine and timely access of effective medicine for the public.

[151] 陳逸南，「專利濫用與學名藥發展」，藥技通訊，第 120 期，頁 25（2008）。

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